



SYSTEMATIC REVIEW

Neoplasms Metastatic to the Larynx: A Systematic Review

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ABSTRACT

Introduction: Metastatic involvement of the larynx from nonhead and neck primary tumors is an exceptionally rare event, frequently misdiagnosed as a primary laryngeal lesion and at risk of inappropriately aggressive surgical management. This systematic review aimed to define the most common primary sources, clinical features, diagnostic workup, treatment, and survival outcomes of tumors metastatic to the larynx from distant sites.

This paper was written by members and invitees of the International Head and Neck Scientific Group.

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Methods: A comprehensive search of PubMed, Web of Science, and Scopus identified original English-language reports published between 1984 and 2026, screened independently by two reviewers according to Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) recommendations.

Results: A total of 83 articles were included, comprising 113 patients with histologically confirmed laryngeal metastases; the evidence consisted exclusively of single case reports and small retrospective series. Patients were predominantly older men with a mean age of 63.6 years. The most frequent primary site was the prostate (26.5%), followed by kidney (18.6%), colorectum (14.2%), skin melanoma (13.3%), lung (8.8%), and breast (6.2%). The supraglottis was the most commonly involved subsite, and the cartilaginous framework was affected in nearly one-quarter of cases. The median interval between primary diagnosis and laryngeal metastasis was 36 months, although the laryngeal lesion preceded or coincided with the primary in roughly one-fifth of patients. Hoarseness, dyspnea or stridor, and dysphagia were the dominant symptoms, clinically indistinguishable from primary laryngeal tumors. Treatment was heterogeneous and largely conservative or palliative, and overall survival was generally measured in months.

Conclusions: Laryngeal metastasis should be suspected whenever a laryngeal mass arises in

a patient with a known or suspected extralaryngeal malignancy, prompting whole-body staging before biopsy and a multidisciplinary, individualized management strategy.

Keywords: Distant metastasis; Secondary laryngeal neoplasms; Nonhead and neck cancer; Systematic review

Key Summary Points

Metastatic spread to the larynx from non-head and neck primary tumors is exceptionally rare and is frequently mistaken for a primary laryngeal carcinoma, exposing patients to unnecessarily aggressive surgery.

The present systematic review, with 83 articles and 113 patients, aimed to define the most common primary sources, clinical features, diagnostic workup, treatment, and survival outcomes of tumors metastatic to the larynx from distant sites.

In this review, prostate adenocarcinoma was the most common primary source, overtaking skin melanoma and renal cell carcinoma reported in older literature; the supraglottis was the most frequently involved subsite, with symptoms (hoarseness, dyspnea/stridor, dysphagia) indistinguishable from those of primary laryngeal tumors.

Because laryngeal metastasis almost always reflects disseminated systemic disease, treatment is largely conservative or palliative and individualized, reserving total laryngectomy only to a minority of patients in which functional and oncological benefits clearly justify such a major intervention. Overall survival is generally measured in months rather than years.

A laryngeal mass arising in a patient with a known or suspected extralaryngeal malignancy should prompt whole-body staging and biopsy with tailored immunohistochemistry before any local intervention.

INTRODUCTION

Metastatic involvement of the larynx from nonhead and neck (HN) primary tumors is an extremely rare clinical entity, accounting for approximately 0.09% to 0.4% of all laryngeal neoplasms [1]. This rarity often leads to clinical misdiagnosis with primary lesions, potentially delaying the identification of an underlying systemic progression, and causing undue aggressive surgical treatments such as total laryngectomy (TL). While the larynx is a well-known primary site for squamous cell carcinomas (SCC), it represents an unusual host for distant localizations due to its anatomical barriers, including a cartilaginous framework and a relatively isolated lymphatic system. From a clinical standpoint, secondaries of the larynx pose a considerable diagnostic challenge, since they present with symptoms mimicking primary tumors of the hypopharynx and larynx, including hoarseness, stridor, dyspnea, dysphagia, otalgia, and globus sensation [2–4].

Historically, the most frequent primaries metastasizing to the larynx are skin (malignant melanoma) and kidney (renal cell carcinoma), followed by gastrointestinal tract, lung, and breast [5, 6]. The dissemination of malignant cells from remote primary sites to the larynx typically proceeds through hematogenous or lymphatic pathways. When traveling via the bloodstream, emboli may follow the systemic circulation through the vena cava or, alternatively, utilize the retrograde route provided by the Batson venous plexus. This valveless vertebral network is characterized by frequent fluctuations and reversals in pressure and flow direction; consequently, it offers a direct conduit for neoplastic spread to the HN that bypasses the traditional filtration of the pulmonary and cardiac systems [7–9]. The distinction between primary and secondary laryngeal neoplasms is crucial, as management strategies and overall prognosis may differ drastically. Most cases of laryngeal distant metastasis are discovered in the context of disseminated systemic disease, making laryngeal involvement a poor prognostic indicator, even though the most recent progresses in the field of immunotherapy, for

example in cutaneous melanoma, have marked an incredible change in terms of life expectancy of such patients with metastatic disease.

This systematic review aims to summarize the current literature to identify the most common primary sources, clinical characteristics, diagnostic workup, treatment, and survival outcomes for patients with secondary laryngeal tumors from distant sites.

METHODS

Search Strategy

This systematic review was performed and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) checklist and statement recommendations [10]. A comprehensive search on PubMed, Web of Science, and Scopus was conducted on February 2026, using the following queries: (laryn* OR glotti* OR subglotti* OR supraglotti* OR transglotti*), AND (metasta* OR distant metastasis OR neoplastic spread OR tumour spread OR tumor spread OR nonhead and neck primar*), AND (tumor* OR tumor* OR malignanc* OR neoplasm* OR cancer* OR carcinoma*), AND NOT (primary laryngeal cancer* OR primary laryngeal carcinoma* OR primary laryngeal tumour* OR primary laryngeal tumor* OR primary laryngeal malignanc*).

Selection Criteria

Only original papers in English, published in a peer-reviewed journal from 1 January 1984 to 15 February 2026, were considered. The starting year 1984 was chosen based on the review by Ferlito and Caruso published in the same year [11]. Exclusion criteria were: (a) nonEnglish articles, (b) studies conducted on nonhuman subjects, (c) papers for which the full text was not available, (d) studies reporting HN primaries or laryngeal primary tumors, and (e) studies related to laryngeal localizations of hematogenous tumors.

Two authors (C.M. and F.E.N.) independently removed duplicate records from the

initial list of titles and screened the remaining records by title and abstract, and, when potentially eligible, by full text, according to the predefined inclusion and exclusion criteria. The reference lists of all included articles were additionally screened, and any further relevant records were assessed by title, abstract, and full text against the same criteria. During patient inclusion, a crossmatching of author names and affiliations with patient-level descriptors (sex, age, primary site and histotype, laryngeal subsite, and interval to laryngeal metastasis) was performed to avoid duplicate cases. Disagreements were solved by discussion between two senior authors (C.P. and A.F.).

Data Extraction

The relevant features (publication year, country, study design) of each study included were collected along with demographics (age at presentation, sex, race), primary tumor features (site, histotype, treatment), metastasis characteristics (laryngeal subsite, endoscopic aspect and vocal fold mobility, time of appearance, symptoms, diagnostic examination), treatment modality, and follow-up details (mean in months and status). Two authors (C.M. and F.E.N.) independently extracted data from eligible articles and created a dedicated database. Data analysis was performed with Microsoft Excel, results were summarized descriptively as frequencies, percentages, means with ranges, and medians. All studies meeting eligibility criteria were included in the descriptive summary; no further subgrouping beyond the primary tumor site was performed. Primary outcomes were distribution of primary tumor site, laryngeal subsite, clinical presentation, treatment modality, and overall survival (OS) from diagnosis of laryngeal metastasis.

The extracted dataset is available from the corresponding author on reasonable request. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Risk of Bias Assessment

Given that the evidence included consisted exclusively of single case reports and small retrospective case series, the overall methodological quality of the literature included is acknowledged as low. These intrinsic limitations, together with the consequent risk of selection, ascertainment, and publication bias, are explicitly addressed in the Discussion section.

RESULTS

General Findings

The initial search retrieved 5676 articles. All details about identification, screening, and inclusion/exclusion criteria are reported in Fig. 1. A total of 83 articles [2, 3, 5, 6, 11–89] were selected for a total of 113 patients with histologically confirmed metastasis to the larynx.

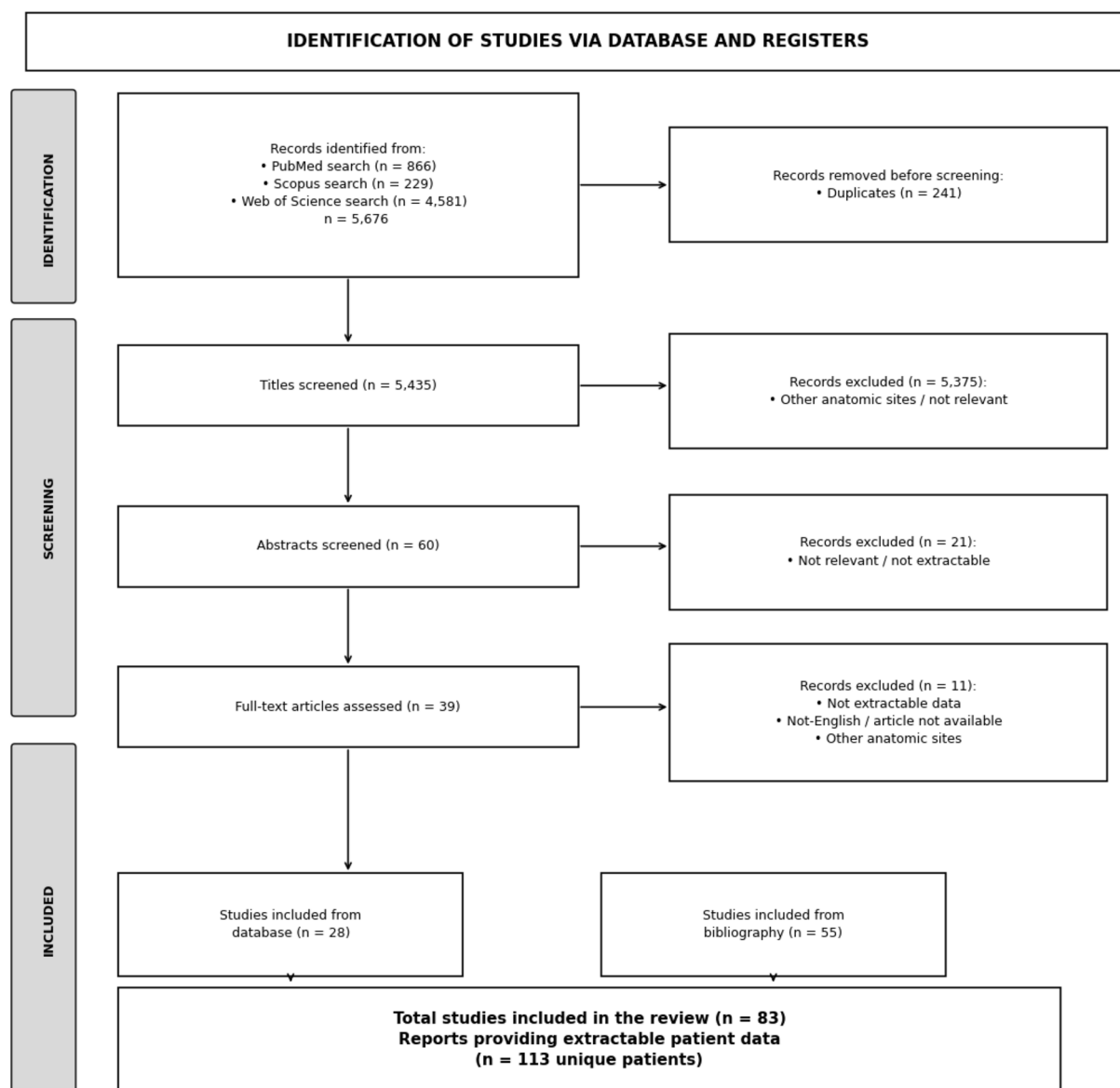


Fig. 1 Article selection

The literature consisted exclusively of single case reports and small retrospective series.

Demographics and Tumor Characteristics

The population ($n = 113$) was predominantly composed of older men [2, 5, 6, 11–13, 15, 17, 19, 22, 24, 26, 28–33, 35–39, 41–43, 45, 47, 49–54, 56, 57, 59–61, 64–67, 70, 71, 73–75, 77–87, 89] (79 of 103 patients in whom sex was reported, corresponding to a male-to-female ratio of 3.3:1), with a mean age at the time of laryngeal metastasis of 63.6 years (range, 29–92). Race reporting was largely unavailable. More details are reported in Table 1.

Primary Tumor Sites and Histology

The distribution of primary tumor sites and their respective histotypes revealed specific patterns of metastatic spread. The most frequent primary was adenocarcinoma of the prostate ($n = 30$, 26.5%) [12, 14, 15, 18, 22, 26, 28, 39, 41, 53, 54, 59, 66, 71, 73, 74, 84, 87, 89]. This was followed by the kidney [14, 17, 19, 24, 28, 29, 35, 38, 43, 52, 56, 63, 65, 67, 70, 75, 77, 78, 82, 85] ($n = 21$, 18.6%), with the clear cell variant of renal cell carcinoma (RCC) being the dominant histotype [17, 19, 24, 28, 29, 35, 38, 52, 63, 67, 70, 75, 77, 78, 82, 85]. Colorectal adenocarcinoma was the third most common source ($n = 16$, 14.2%) [2, 3, 5, 20, 32–34, 37, 44, 46, 47, 55, 62, 64, 81], followed by cutaneous melanoma ($n = 15$, 13.3%) [6, 11, 13, 14, 23, 40, 49, 57, 83], lung cancer ($n = 10$, 8.8%) [25, 31, 32, 51, 60, 69, 79, 80, 86, 88], and breast cancer ($n = 7$, 6.2%) [14, 27, 48, 68, 76, 79]. Less frequent primary sites included ovary [14, 21, 72] and bone [30, 36, 42] (three patients each, 2.7%), stomach ($n = 2$, 1.8%) [14, 79], and single cases originating in the pancreas [16], soft tissues of the lower extremity [45], liver [50], uterus [58], chest wall [61], and urinary bladder [79]. Histologically, adenocarcinoma was the dominant entity, accounting for 41 patients (36.3%) [2, 3, 5, 12, 14–16, 20, 25–28, 32–34, 37, 39, 44, 46, 47, 54, 55, 58, 59, 62, 64, 66, 71, 73, 79, 81, 84, 86–89], followed by clear cell RCC (14.2%) [17, 19, 24, 28, 29, 35, 38, 52, 63, 67, 70, 75, 77, 78,

82, 85], and melanoma (13.3%) [6, 11, 13, 14, 23, 40, 49, 57, 83], including two amelanotic variants [6, 23]. Rarer histotypes, such as chondroma [36], hepatocellular [50], anaplastic [21], high-grade serous [72], urothelial carcinomas [79], and poorly differentiated non-small cell lung cancer [80], contributed isolated observations (Fig. 2).

Laryngeal Subsite and Timing of Appearance

The supraglottis was the most common location for metastatic spread ($n = 26$, 23.0%) [6, 11, 13, 15, 16, 23, 28, 31, 35, 38, 40, 43, 45, 49, 50, 57, 60, 64, 76, 78, 80, 86, 89], followed by the glottis [17, 18, 25, 26, 29, 32, 34, 39, 42, 52, 63, 67, 70, 81, 83, 88] and subglottis [2, 3, 12, 13, 19–21, 24, 27, 32, 44, 55, 58, 62, 69, 87] ($n = 17$ each, 15.0%). Transglottic involvement was described in 15 cases (13.3%) [5, 22, 33, 36, 37, 46–48, 53, 56, 61, 68, 72, 77, 85], while the subsite was not specified in 11 (9.7%) [14, 65]. The cartilaginous framework (thyroid, cricoid, and arytenoid cartilages) and, when contiguous, the hyoid bone was involved in 27 patients (23.9%) [28, 30, 41, 51, 54, 59, 66, 71, 73–75, 79, 82, 84] most frequently in patients with prostate, breast, kidney, and lung primaries (Table 2).

The timing of appearance of laryngeal metastases showed wide variability. The median interval between diagnosis of the primary tumor and laryngeal metastasis was approximately 36 months (mean, 60.3 months; range, 1–276) in the 62 patients for whom this interval was reported [2, 3, 5, 6, 11–13, 15–17, 19–40, 42–50, 52–73, 75–79, 83, 85, 87, 88]. Notably, in 12 (10.6%) [15, 19, 21, 24, 28, 29, 37, 38, 50, 77, 82] patients, the laryngeal lesion preceded the diagnosis of the primary tumor and represented the index symptom of an occult visceral malignancy, most often RCC or prostatic adenocarcinoma [15, 19, 24, 28, 29, 38, 77, 82]. In 13 additional patients (11.5%) [16, 32, 47, 60, 67, 73, 74, 79, 80, 89], the laryngeal and primary lesions were diagnosed synchronously. Concomitant distant disease was documented in 74 patients (65.5%), most commonly in bone ($n = 44$) [18, 22, 23, 26, 27, 30, 36–39, 41, 42, 44, 45, 47–49, 51, 53, 54, 59, 61, 63, 64, 68, 73, 74, 77,

Table 1 Articles included and demographic data

Ref.	Journal	Year	Title	Country	No. of cases	Age	Sex	Origin site
Ferlito and Caruso [11]	“ORL J Otorhinolaryngol Relat Spec”	1984	Secondary malignant melanoma of the larynx. Report of two cases and review of 79 laryngeal secondary cancers	Italy	1	75	F	Skin (check)
Coakley and Ranson [12]	“J Laryngol Otol”	1984	Metastasis to the larynx from a prostatic carcinoma. A case report	England	1	64	M	Prostate
Morgan et al. [13]	“Laryngoscope”	1985	Palliative laser surgery for melanoma metastatic to the larynx: report of two cases	USA	1	42	M	Skin (chest)
Batsakis et al. [14]	“Head Neck Surg”	1985	Metastases to the larynx	USA	3	NA	NA	Skin
					2	NA	NA	Breast
					2	NA	NA	Kidney
					1	NA	NA	Prostate
					1	NA	NA	Ovary
					1	NA	NA	Stomach
Hessan et al. [15]	“Laryngoscope”	1986	Urogenital tract carcinoma metastatic to the head and neck	USA	1	70	M	Prostate
Yeatman et al. [16]	“Laryngoscope”	1986	A rare manifestation of metastatic adenocarcinoma	USA	1	51	F	Pancreas

Table 1 continued

Ref.	Journal	Year	Title	Country	No. of cases	Age	Sex	Origin site
Maung et al. [17]	"J Otolaryngol"	1987	Metastatic renal carcinoma to larynx	Canada	1	48	M	Kidney
Tetu et al. [18]	"Cancer"	1987	Small cell carcinoma of the prostate. Part I. A clinicopathologic study of 20 cases	USA	1	70	M	Prostate
Ferlito et al. [19]	"J Laryngol Otol"	1987	Metastasis to the larynx revealing a renal cell carcinoma	Italy	1	73	M	Kidney
Ferlito et al. [6]	"Arch Otolaryngol Head Neck Surg"	1988	Secondary laryngeal tumors	Italy	1	71	M	Skin (back)
Cavicchi et al. [20]	"J Laryngol Otol"	1990	Laryngeal metastasis from colonic adenocarcinoma	Italy	1	52	M	Skin (check)
						62	M	Skin (leg)
						59	F	Colorectal
Cullen [21]	"J Laryngol Otol"	1990	Ovarian carcinoma metastatic to the larynx	Ireland	1	71	F	Ovary
Grignon et al. [22]	"Urology"	1990	Carcinoma of prostate metastasizing to vocal cord	USA	1	71	M	Prostate
Ikeda et al. [23]	"J Laryngol Otol"	1991	Amelanotic melanoma metastatic to the epiglottis	Japan	1	42	M	Skin
Greenberg et al. [24]	"Urology"	1992	Hoarseness: a unique clinical presentation for renal cell carcinoma	USA	1	55	M	Kidney

Table 1 continued

Ref.	Journal	Year	Title	Country	No. of cases	Age	Sex	Origin site
Ogata et al. [25]	"Jpn J Clin Oncol"	1993	Laryngeal metastasis from a pulmonary papillary adenocarcinoma: a case report	Japan	1	59	F	Lung
Park YW. and Park M.H. [26]	"Head Neck"	1993	Vocal cord paralysis from prostatic carcinoma metastasizing to the larynx	USA	1	66	M	Prostate
Wanamaker et al. [27]	"Head Neck"	1993	Manifestation of metastatic breast carcinoma to the head and neck	USA	1	77	F	Breast
Mochimatsu et al. [28]	"J Laryngol Otol"	1993	Tumours metastasizing to the head and neck—a report of seven cases	JAPAN	1	64	M	Kidney
Marlowe et al. [29]	"Neuroradiology"	1993	Metastatic hyper-nephroma to the larynx: an unusual presentation	USA	1	64	M	Prostate
Shimizu et al. [30]	"Ann Otol Rhinol Laryngol"	1994	Osteosarcoma metastatic to the larynx	USA	1	51	M	Bone (tibia)
Bernaldez et al. [31]	"J Laryngol Otol"	1994	Pulmonary carcinoma metastatic to the larynx	Spain	1	56	M	Lung
Nicolai et al. [32]	"Laryngoscope"	1996	Metastatic neoplasms to the larynx: report of three cases	Italy	1	69	M	Lung
					1	53	F	Colorectal
					1	58	F	Colorectal

Table 1 continued

Ref.	Journal	Year	Title	Country	No. of cases	Age	Sex	Origin site
Puxeddu et al. [33]	"Eur Arch Otorhinolaryngol"	1997	Colon adenocarcinoma metastatic to the larynx	Italy	1	65	M	Colorectal
Hilger et al. [34]	"J Laryngol Otol"	1998	Adenocarcinoma of the larynx—a distant metastasis from a rectal primary	England	1	73	F	Colorectal
Dee et al. [35]	"Arch Pathol Lab Med"	2000	Laryngeal metastasis 7 years after radical nephrectomy	USA	1	48	M	Kidney
Fischbein et al. [36]	"J Comput Assist Tomogr"	2000	Metastatic chordoma to the larynx in a patient presenting with hoarseness	USA	1	49	M	Bone (sacrum and coccyx)
Danikas et al. [37]	"Am Surg"	2000	Unusually aggressive recurrent carcinoid metastasizing to larynx, pancreas, adrenal glands, and brain	USA	1	79	M	Colorectal
Navarro et al. [38]	"Tumori"	2000	Metastatic renal cell carcinoma to the head and neck area	Spain	1	83	M	Kidney
Apostolides et al. [39]	"J Otolaryngol"	2000	Prostatic adenocarcinoma metastasizing to the vocal folds	Canada	1	82	M	Prostate
Pau et al. [40]	"J Laryngol Otol"	2001	Metastatic malignant melanoma of the larynx	USA	1	78	F	Skin (calf)

Table 1 continued

Ref.	Journal	Year	Title	Country	No. of cases	Age	Sex	Origin site
Prescher et al. [41]	"Laryngoscope">	2002	Laryngeal prostatic cancer metastases: an underestimated route of metastases?	Germany	1	77	M	Prostate
					1	78	M	Prostate
					1	67	M	Prostate
					1	87	M	Prostate
					1	75	M	Prostate
					1	72	M	Prostate
Saleem et al. [42]	"J Otolaryngol"	2002	Osteogenic sarcoma metastasizing to the larynx	Saudi Arabia	1	29	M	Bone (lower extremity)
Rossini et al. [43]	"Otolaryngol Head Neck Surg"	2004	Renal cell carcinoma metastatic to the larynx	Italy	1	54	M	Kidney
Sano et al. [44]	"Acta Otolaryngol">	2005	A case of metastatic colon adenocarcinoma in the larynx	Japan	1	81	F	Colorectal
Daly et al. [45]	"Ear Nose Throat J"	2006	Lower-extremity liposarcoma metastatic to the larynx: case report	USA	1	46	M	Soft tissue (lower extremity)
Marioni et al. [46]	"Acta Otolaryngol"	2006	Laryngeal metastasis from sigmoid colon adenocarcinoma followed by peristomal recurrence	Italy	1	78	F	Colorectal
Ramanathan et al. [47]	"Ear Nose Throat J"	2007	Laryngeal metastasis from a rectal carcinoma	Malaysia	1	51	M	Colorectal

Table 1 continued

Ref.	Journal	Year	Title	Country	No. of cases	Age	Sex	Origin site
Grasso et al. [48]	"J Clin Oncol"	2007	Vocal cord metastasis from breast cancer	Italy	1	66	F	Breast
Lanson et al. [49]	"Curr Oncol"	2010	Malignant melanoma metastatic to the larynx: treatment and functional outcome	USA	1	61	M	Skin (supraclavicular)
Hinojar-Gutiérrez et al. [50]	"Rev Esp Enferm Dig"	2011	Laryngeal metastasis as first presentation of hepatocellular carcinoma	Spain	1	55	M	Liver
Ta and Kim [2]	"Ear Nose Throat J"	2011	Rectal adenocarcinoma metastatic to the larynx	USA	1	60	M	Colorectal
Ozcan Kara et al. [51]	"Mol Imaging Radionucl Ther"	2011	Rare thyroid cartilage and diaphragm metastases from lung cancer visualized on F-18 FDG-PET/CT imaging	Turkey	1	49	M	Lung
Mehdi et al. [52]	"Gulf J Oncolog"	2012	Renal cell carcinoma metastasizing to larynx: a case report	Oman	1	57	M	Kidney
Karime et al. [53]	"Ear Nose Throat J"	2012	Prostate cancer metastatic to the larynx: a case report	USA	1	71	M	Prostate
Oliveira et al. [54]	"Braz J Otorhinolaryngol"	2012	Laryngeal metastasis of a prostate carcinoma: one rare entity	Brazil	1	73	M	Prostate

Table 1 continued

Ref.	Journal	Year	Title	Country	No. of cases	Age	Sex	Origin site
Chen et al. [55]	"Clin Nucl Med"	2012	Asymptomatic metastasis to the larynx detected by FDG PET/CT in a patient with recurrent rectal adenocarcinoma	Taiwan	1	72	F	Colorectal
Demir et al. [56]	"Can Urol Assoc J"	2012	Metastases of renal cell carcinoma to the larynx and thyroid: two case reports on metastasis developing years after nephrectomy	Turkey	1	60	M	Kidney
Arabi Mianroodi et al. [57]	"Ear Nose Throat J"	2013	Malignant melanoma metastatic to the larynx: a case report	Iran	1	62	M	Skin (tragus)
Lee et al. [58]	"J Palliat Med"	2014	Metastatic endometrial adenocarcinoma to the larynx: a case report and discussion of upper airway management	Taiwan	1	55	F	Uterus
Terashima [3]	"Fukushima J. Med. Sci"	2014	Long-term survival after resection of metastases in the lungs and larynx originating from sigmoid colon cancer: report of a case	Japan	1	64	F	Colorectal

Table 1 continued

Ref.	Journal	Year	Title	Country	No. of cases	Age	Sex	Origin site
Ng et al. [59]	"Jpn J Radiol"	2015	Asymptomatic metastasis to cricoid from prostate carcinoma: an incidental finding detected on 18F-choline PET/CT	Singapore	1	58	M	Prostate
Kalai et al. [60]	"Lung India"	2015	Laryngeal metastasis from lung cancer	India	1	29	M	Lung
Singhal et al. [61]	"J Cancer Res Ther"	2015	Chondrosarcoma of chest wall metastasising to the larynx: case report and review of literature	India	1	30	M	Chest wall
Zenga et al. [5]	"J Voice"	2016	Metastatic cancer to the larynx: a case report and update	USA	1	52	M	Colorectal
Heyes et al. [62]	"Case Rep Otolaryngol"	2017	Subglottic metastatic rectal adenocarcinoma: a specialist multidisciplinary airway team approach for optimized voice and airway outcome	England	1	56	F	Colorectal
Nielsen and Swan [63]	"Case Studies in Surgery"	2017	Renal cell carcinoma metastasis to the vocal cord: a case report	Iraq	1	57	F	Kidney
Bracanovic et al. [64]	"Balkan Med J"	2017	Hyoid bone and thyroid cartilage metastases from sigmoid colon adenocarcinoma: a case report	Serbia	1	63	M	Colorectal

Table 1 continued

Ref.	Journal	Year	Title	Country	No. of cases	Age	Sex	Origin site
Liou et al. [65]	"Laryngoscope"	2018	Survival of renal cell carcinoma metastatic to nonthyroid head and neck region: a systematic review	USA	1	68	M	Kidney
Olvera et al. [66]	"Case Rep Med"	2018	Unusual presentation of prostate cancer metastatic to the cricoid cartilage and oral cavity	Mexico	1	68	M	Prostate
Garrido-Abad and García-Martín [67]	"N Engl J Med"	2019	Vocal cord metastasis	Spain	1	49	M	Kidney
Kumar R. et al. [68]	"Curr Probl Cancer"	2019	Laryngeal metastases from breast cancer: a rare clinical entity	India	1	63	F	Breast
Yano et al. [69]	"Clin Pract Cases Emerg Med"	2019	Endotracheal metastasis causing airway obstruction	Japan	1	73	F	Lung
Rashid et al. [70]	"Urol Case Rep"	2019	Metastasis of renal cell carcinoma to the vocal cord ten years after radical nephrectomy: a case report	Iraq	1	74	M	Kidney

Table 1 continued

Ref.	Journal	Year	Title	Country	No. of cases	Age	Sex	Origin site
Annovazzi et al. [71]	"Clin Nucl Med"	2020	Asymptomatic metastasis to thyroid cartilage detected by 18F-choline and 64Cu-PSMA PET/CT as a single site of disease relapse in a patient with castration-resistant prostate carcinoma	Italy	1	83	M	Prostate
Purcell et al. [72]	"Case Rep Surg"	2020	Ovarian cancer metastasis to the larynx: a case report and review of the literature	Canada	1	65	F	Ovary
Tupalli et al. [73]	"Nucl Med Mol Imaging"	2020	An unusual case of simultaneous cricoid and thyroid cartilage metastases from prostatic adenocarcinoma on 68 Ga-PSMA PET/CT	India	1	65	M	Prostate
Gupra et al. [74]	"Indian J Nucl Med"	2021	Metastatic thyroid cartilage lesion from prostatic adenocarcinoma on 68 Ga-prostate specific membrane antigen positron emission tomography computed tomography scan: case series	India	1	65	M	Prostate
					1	92	M	Prostate
					1	54	M	Prostate

Table 1 continued

Ref.	Journal	Year	Title	Country	No. of cases	Age	Sex	Origin site
Vrebac et al. [75]	"Med Flum"	2021	Metastasis of clear cell renal cell carcinoma to the larynx: a short literature review and presentation of a rare case of prolonged survival	Croatia	1	72	M	Prostate
Stefanidis A. et al. [76]	"Oral Oncol"	2021	P-220 case report: laryngeal metastasis of breast cancer	Greece	1	43	F	Breast
Baba et al. [77]	"Radiol Case Rep"	2021	CT and MR imaging of laryngeal metastasis from renal cell carcinoma: a case report	Japan	1	80	M	Kidney
Eastwood et al. [78]	"Br J Hosp Med (Lond)"	2021	A rare case of isolated laryngeal metastasis 23 years after nephrectomy for clear cell renal carcinoma	England	1	84	M	Kidney
Gupta et al. [79]	"Indian J Nucl Med"	2021	Rare thyroid cartilage metastases detected on 18F-fluorodeoxyglucose positron emission tomography/computed tomography scan	India	1	58	M	Lung
					1	63	F	Breast
					1	42	M	Stomach

Table 1 continued

Ref.	Journal	Year	Title	Country	No. of cases	Age	Sex	Origin site
Gao et al. [80]	"Clin Nucl Med"	2022	Pulmonary sarcomatoid carcinoma with epiglottitis and ileum metastasis detected by 18 F-FDG PET/CT	China	1	56	M	Bladder
Aljariri et al. [81]	"Clin Case Rep"	2023	Metastatic sigmoid adenocarcinoma to the larynx: a case report and updated literature review	Qatar	1	60	M	Colorectal
Ahmed et al. [82]	"Cureus"	2023	Metastatic renal cell carcinoma masquerading as a laryngeal tumor: a case report	India	1	66	M	Kidney
Ciolofoan et al. [83]	"Life (Basel)"	2023	Cutaneous malignant melanoma metastatic to the larynx and trachea: a case report and review of the literature	Romania	1	56	M	Skin (nuchal region)
Loyal et al. [84]	"World J Nuclear Med"	2024	Thyroid cartilage metastases from prostate cancer on 18F PSMA PET CT: a case series	Kenya	1	68	M	Prostate
					1	81	M	Prostate
					1	88	M	Prostate

Table 1 continued

Ref.	Journal	Year	Title	Country	No. of cases	Age	Sex	Origin site
Sanchez Teran et al. [85]	“BMJ Cas Rep”	2024	Renal cell carcinoma (RCC) spreading to the larynx: an unusual condition	Mexico	1	MID-70S	M	Kidney
Maglione et al. [86]	“Indian J Otolaryngol Head Neck Surg”	2024	Rare primitive lung adenocarcinoma in larynx: a case report	Italy	1	63	M	Lung
Bosco et al. [87]	“Ear Nose Throat J”	2024	A unique case of metastatic prostate carcinoma to the subglottis	USA	1	85	M	Prostate
Kim et al. [88]	“Ear Nose Throat J”	2025	Lung adenocarcinoma metastasis to the vocal cord	Korea	1	75	F	Lung
İlkiz et al. [89]	“Turk Arch Otorhinolaryngol”	2025	Laryngeal metastasis of prostate adenocarcinoma: a case report	Turkey	1	80	M	Prostate

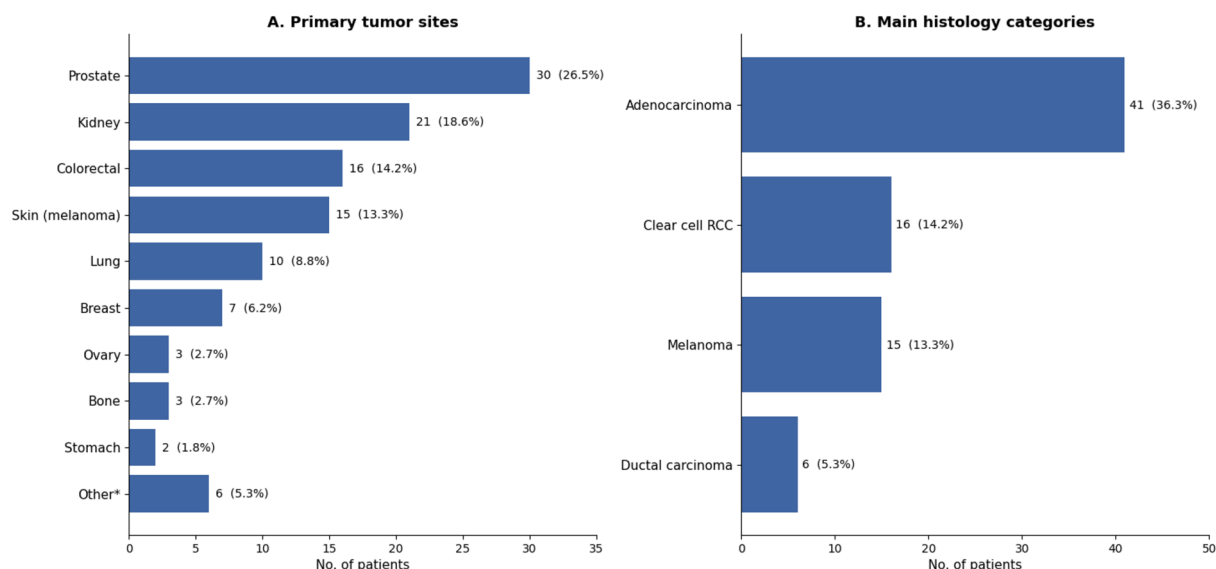


Fig. 2 Primary tumor site and main histology categories. *Other primary site: single cases of bladder, pancreas, soft tissue, uterus, liver, and chest wall

84, 87, 89] and lung ($n = 33$) [2, 3, 5, 11, 18–20, 23, 28, 30, 32, 33, 37, 38, 42–44, 46, 48, 49, 53, 58, 61–63, 67, 68, 74, 76, 81, 84], confirming the highly disseminated nature of the neoplasm at the time of laryngeal involvement.

Clinical Presentation and Diagnosis

The most frequent presenting complaint was hoarseness, reported in 46 patients (40.7%) [11, 13, 15, 17, 19, 20, 22, 24–26, 28, 29, 31–36, 38, 39, 42, 44, 45, 48, 53, 54, 56, 57, 62, 63, 66–68, 70, 72, 75, 81, 82, 85–89], followed by respiratory symptoms such as dyspnea or stridor in 28 (24.8%) [2, 12, 13, 20, 21, 27, 32–34, 40, 44, 53, 54, 58, 60, 62, 66, 68, 69, 76, 79, 85–87], while dysphagia was reported in 12 (10.6%) [6, 16, 31, 37, 43, 45, 57, 76, 78, 86]. In 11 patients (9.7%) [5, 6, 41, 50, 52, 59], the laryngeal lesion was clinically silent and discovered during routine staging imaging (Fig. 3). Endoscopic data were available for 68 of 113 patients (60.2%). The most frequently observed pattern was an exophytic, hypervascularized, or polypoid growth noted in 34 cases (30.1%) [11, 13, 17, 19, 20, 23, 25, 29, 31, 32, 35, 38–40, 43, 44, 46, 47, 57, 60, 62, 63, 67, 70, 76–78, 83, 88]. Submucosal

mass or swelling was the second most common presentation, identified in 18 patients (15.9%) [3, 12, 16, 21, 22, 24, 26–28, 32, 33, 45, 50, 53, 58, 69, 72, 87, 89], while pigmented lesions [13, 49], often associated with melanoma, and ulcerative lesions [52, 86] accounted for two cases each (1.8%). In nine cases (8.0%), no obvious endolaryngeal mass was visible at endoscopy [2, 5, 30, 34, 36, 42, 54, 66, 68]. Vocal cord mobility was assessable in 65 patients: of these, 26.2% ($n = 17$) presented laryngeal mobility impairment, including fixed ($n = 11$, 16.9%) [26, 27, 32–34, 36, 37, 47, 53, 54, 81] or hypomobile vocal cords ($n = 6$, 9.2%) [42, 57, 68, 72, 75, 87] (Table 2). Diagnosis was confirmed by pretreatment biopsy in 61 patients (70.1% of all subjects with these data) [2, 5, 11, 12, 15–17, 19, 22, 24–29, 31–34, 36, 37, 39, 42, 44, 47, 49, 50, 52–60, 62, 66–69, 71, 72, 75, 77–83, 85–89], while in 26 (29.9%) [6, 13, 20, 23, 30, 35, 38, 40, 41, 43, 46, 48, 63, 70, 76], the diagnosis was reached on the surgical specimen or at postmortem examination. Specific neck imaging was performed in 58 patients (CT in 54 [2, 5, 13, 16, 17, 23, 24, 26, 27, 29, 31–34, 37–39, 44–48, 50, 52–54, 56–61, 64, 66, 69, 72, 77–82, 89], and MR in 8 [27, 29, 30, 36, 38, 59, 71, 76], both in 4 [27, 29, 38, 59]), while a whole-body examination with PET/CT was

Table 2 Distribution by laryngeal subsite, endoscopic appearance, and vocal cord impairment

Laryngeal subsite	N (%)	Exophytic/ vascular/ polypoid	Edema/ submucosal mass	Pigmented	Ulcerative	No obvious mass	Endo NA	No impair- ment	Hypomobility	Fixed	MOBNA
Supraglottis	26 (23.0%)	12	4	1	1	0	8	18	1	0	7
Glottis	17 (15.0%)	9	2	1	0	4	1	7	2	4	4
Subglottis	17 (15.0%)	9	4	0	1	1	2	11	1	1	4
Transglottis	15 (13.3%)	4	6	0	0	2	3	4	2	5	4
Laryngeal skeleton	27 (23.9%)	0	2	0	0	2	23	5	0	1	21
Not reported	11 (9.7%)	0	0	0	0	0	11	0	0	0	11
Total	113 (100%)	34 (30.1%)	18 (15.9%)	2 (1.8%)	2 (1.8%)	9 (8.0%)	48 (42.5%)	45 (39.8%)	6 (5.3%)	11 (9.7%)	51 (45.1%)

done in 23 patients (20.4%) [42, 49, 55, 59, 68, 73–75, 79, 80, 85–89].

Laryngeal Treatment and Survival

Therapeutic strategies were extremely heterogeneous and mirrored the palliative intent of most interventions. Conservative laryngeal surgery (including transoral laser or robotic excision and open partial laryngectomies) was performed in 24 patients (21.2%) [2, 3, 13, 17, 19, 20, 23, 25, 29, 32, 36, 38, 43, 48, 49, 55, 57, 58, 62, 63, 67, 70, 82, 86, 88], while TL was undertaken more rarely ($n = 11$, 9.7%): 6 as primary treatment [15, 31, 37, 45, 46, 50], and 5 after other palliative measures (radiotherapy [RT], chemotherapy [CHT], target therapy, or airway-securing tracheotomy) [24, 32, 34, 65, 85]. Adjuvant treatment was performed in nine cases [3, 6, 13, 30, 49, 58, 85]. A nonsurgical curative approach (chemoradiotherapy [CRT], immunotherapy, or targeted therapy) was taken in 26 patients (23.0%) [2, 11, 22, 24, 26, 27, 32, 39, 52–54, 59, 60, 65, 66, 68, 69, 71, 75, 78, 80, 83, 87, 89]. Airway-securing tracheotomy was performed in 14 (12.4%) patients: in four cases as exclusive treatment [12, 21, 44, 61], in seven in association with (C)RT [2, 5, 33, 53, 66, 69, 87], and in three, such an emergent airway procedure was followed by TL [24, 34, 85]. Palliative or no laryngeal treatment was reported for 12 patients (10.6%) [5, 16, 28, 33, 41, 42, 47, 56, 64, 72, 81], while for 24.8%, there were no data [6, 11, 14, 18, 28, 51, 73, 74, 79, 84]. Follow-up was available for 62 patients: 19 (30.6%) were alive with disease (AWD) [2, 5, 16, 18, 25, 32, 43–46, 49, 50, 54, 56, 65–67, 80, 83], 16 (25.8%) died of disease (DOD) [11, 13, 15, 19, 21, 23, 27, 32–34, 42, 63, 81, 89], 8 (12.9%) died of unrelated causes (DOC) [31, 37, 41], 2 (3.2%) died for unknown causes [57, 77], 14 (22.6%) showed no evidence of disease at the last observation (NED) [3, 13, 17, 20, 24, 30, 38, 52, 58, 62, 69, 75, 82, 85], and 3 (4.8%) [28, 53, 60] were lost to follow-up. Mean OS calculated from the diagnosis of laryngeal metastasis, available for 48 patients, was 48.9 months (range, 0–204). Additional details are reported in Table 3.

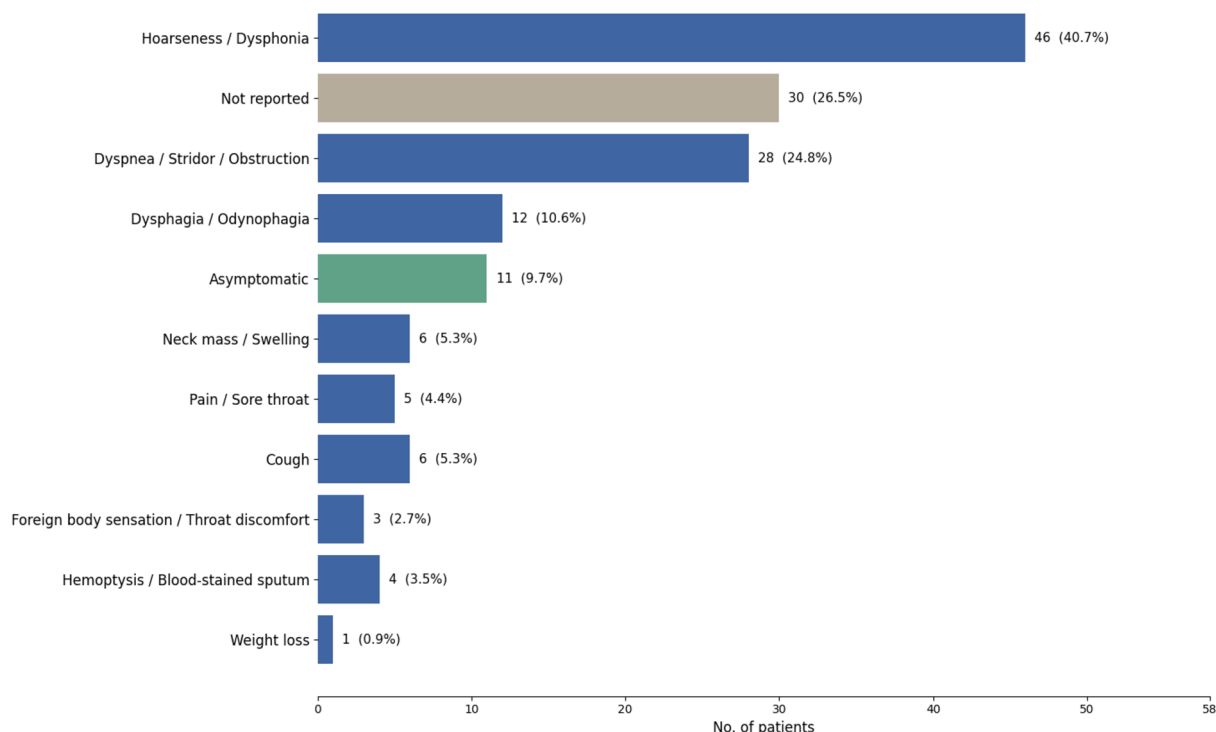


Fig. 3 Presenting symptoms

DISCUSSION

Metastatic spread to the larynx represents an uncommon clinical occurrence, as already established in previous studies [5, 11, 14]. The current systematic review, collecting 83 publications and 113 cases published over more than 40 years, is one of the largest reviews on this topic and provides a chance to revisit well-established assumptions through the contemporary oncological practice.

The cohort was predominantly composed by men and clustered in the sixth and seventh decades of life, in agreement with data provided by older reviews [6, 14]. The higher proportion of men can be partly explained by the underlying histological nature of the cohort. Prostate cancer accounted for about 26.5% of cases, while RCC, with a male-to-female incidence of 2:1, made up an additional 18.6%. The higher age distribution observed is consistent with the natural history of visceral cancers,

in which stage IV is usually associated with a late diagnosis and older age [90, 91].

Classical case series have consistently considered cutaneous melanoma and RCC, followed by gastrointestinal tract, lung, and breast carcinomas, as the most frequent primaries metastasizing to the larynx [6, 33, 44, 92]. Our findings partially modify this assumption. Skin (melanoma), kidney, and colorectum remain prominent primaries (13.3%, 18.6%, and 14.2%, respectively), even though the prostate ($n = 30$, 26.5%) appears considerably more represented than in the older literature (about 5%) [93, 94]. This shift could be related to the recent rising prevalence of clinically detected prostate adenocarcinoma and progressive aging of Western populations [95]. Moreover, modern systemic regimens (such as hormone therapy or immunotherapy) have prolonged survival in men with advanced prostate cancer and consequently increased the time during which unusual metastatic deposits can become clinically

Table 3 Laryngeal treatment details and follow-up status

Treatment category		
Surgery		
Conservative surgery	24	21.2%
Total laryngectomy (TL)—total	11	9.7%
—TL as primary treatment	6	5.3%
—TL after other treatments (RT, tracheotomy, target therapy)	5	4.4%
Surgery NOS	8	7.1%
Tracheotomy for airway securing (no TL)		
Tracheotomy alone	4	3.5%
Tracheotomy + RT	3	2.7%
Tracheotomy + RT + hormone therapy	1	0.9%
Tracheotomy + CRT	2	1.8%
Tracheotomy + hormone therapy	1	0.9%
Nonsurgical treatment		
CHT alone	5	4.4%
RT alone	4	3.5%
CRT alone	2	1.8%
CHT + RT	2	1.8%
Target therapy/immunotherapy	4	3.5%
Hormonal therapy + RT	1	0.9%
Hormonal therapy alone	1	0.9%
Other		
No treatment (none/BSC/palliative care)	12	10.6%
Not reported (NA)	28	24.8%
Total	113	100%
Follow-up status		
NED	14	22.6%
AWD	19	30.6%
DOD	16	25.8%
DOC	8	12.9%
DOC/DOD	2	3.2%

Table 3 continued

Treatment category		
Surgery		
Lost	3	4.8%
Total	62	100%

or radiologically evident [96, 97]. However, this finding should be interpreted with caution. Because the literature consists exclusively of case reports and small series, it is highly susceptible to publication and ascertainment bias; the apparent predominance of prostate cancer may therefore reflect selective reporting rather than a true shift in the biology of laryngeal metastasis.

The supraglottis was by far the most commonly involved subsite. This distribution, as previously reported in the literature, reflects the anatomical arrangement of laryngeal lymphatic drainage and blood circulation, which is well developed around the preepiglottic and paraglottic spaces [6, 32]. The low incidence of true vocal cord metastases therefore mirrors the well-known pattern observed in primary glottic SCC. For what concerns metastases to the cartilaginous framework (23.9% thyroid, cricoid, and arytenoid cartilages and, when contiguous, the hyoid bone in our systematic review), they most frequently arise in the portion undergoing ossification, consistent with a hematogenous spread favored by the rich vascular supply of the ossified, marrow-containing cartilage [94].

Most patients presented with metachronous deposits that were diagnosed months to years after treatment of the primary tumor, with a median interval of 36 months. Synchronous presentation or laryngeal tumor preceding the diagnosis of the primary lesion were less common (9.9% and 10.8%, respectively).

Symptoms at presentation were dominated by hoarseness (40.7%), dyspnea or stridor (24.8%), and dysphagia or odynophagia (10.6%). These symptoms are indistinguishable from those derived from primary laryngeal tumors, and, as a result, no clinical sign at initial presentation allows the physician to suspect a metastatic origin of the lesion observed.

A small subgroup (9.7%) was entirely asymptomatic, and the laryngeal lesion was incidentally discovered during staging or imaging for oncological surveillance. In contrast, about one of seven patients presented with severe airway obstruction requiring urgent management, thus highlighting the relatively rapid clinical progression of many of these lesions.

At endoscopy, the most frequent appearance was that of an exophytic, polypoid, or hypervascularized “mulberry-like” mass (30.1%), a pattern particularly characteristic of RCC [19, 38, 43, 63, 70, 77]. Submucosal swellings or diffuse edema accounted for 15.9% of cases, mimicking chronic laryngitis, Reinke’s edema, or amyloidosis, thus leading to further diagnostic delay. This insidious pattern was typically encountered in adenocarcinomatous metastases from prostate, breast, or colorectal primaries [16, 28, 32, 33]. Pigmented lesions are pathognomonic of melanoma [13, 49], raising the differential diagnosis between primary mucosal melanoma and skin metastatic disease. This finding, together with the possibility of synchronous presentation or initial manifestation of a non-HN tumor, may have practical implications: the detection of a laryngeal lesion with atypical features (highly vascular, pigmented, or submucosal) in a patient with or without a significant smoking history should always prompt whole-body staging prior to an adequate biopsy (CT or MRI of the neck combined with CT of the chest and abdomen–pelvis, or whole-body 18F-FDG PET/CT). The extent of systemic staging should be proportionate to the clinical context: a limited targeted workup may suffice when the primary is already known and controlled, whereas a broader whole-body evaluation is warranted when the laryngeal lesion is the index presentation of an occult malignancy. Such cross-sectional imaging should ideally precede or accompany biopsy, to both plan a safe procedure (hypervascular deposits from renal cell carcinoma or melanoma carry a nonnegligible bleeding risk) and to orient the pathologist toward the most informative immunohistochemical panel.

Imaging information cannot reliably distinguish metastatic deposits from a primary laryngeal tumor, and definitive diagnosis always relies on histological examination with a tailored immunohistochemical panel.

Because laryngeal metastases typically occur in the setting of advanced, disseminated disease, treatment strategies are largely dictated by the extent of the primary tumor, burden of systemic disease, and the patient’s overall clinical condition and performance status. In our series, airway-securing tracheotomy was performed in 14 (12.4%) subjects: 4 as an exclusive treatment, 7 in association with C(RT), and 3 followed by TL. The most frequent single local intervention was, however, conservative surgical resection, and reserved to the small subset of patients (21.2%) with a solitary metachronous lesion and well-controlled primary disease. TL was performed only in a minority of patients (9.7%), since this procedure carries a substantial impact on quality of life and must therefore be reserved to carefully selected cases in which functional and oncological benefits clearly justify such a major intervention. Nonsurgical care ([C]RT, hormone therapy, immunotherapy, or targeted therapy) was the treatment of choice in 26 patients (23.0%). Survival data, although inconsistently reported, confirmed the prognostic severity of this condition: for the majority of patients, in fact, such a diagnosis translated into a median survival of months rather than years, in line with the high stage of the underlying disease. Exceptions to this rule were concentrated in two subgroups: patients with RCC not metastatic elsewhere except for the larynx and a smaller group of well-controlled adenocarcinoma (often colorectal) that was amenable to complete local resection or modern systemic therapy. These observations collectively suggest that aggressive local treatment of a laryngeal metastasis should be considered only when it can be integrated into a coherent multidisciplinary therapeutic plan aimed at improving quality of life or, in carefully selected cases, at achieving oligometastatic disease control.

The present review has several limitations. Most reports are in fact individual cases or very small series published over a period of more

than 40 years, selected evidence intrinsically prone to publication and reporting bias: cases that are clinically unusual, surgically interesting, or therapeutically successful are more likely to be published, whereas less informative or anecdotal observations are systematically underrepresented. As a consequence, the true incidence of laryngeal metastasis remains impossible to derive from the published literature. Moreover, the restriction to English-language full-texts may have introduced further selection bias. Data on follow-up, treatment details, and survival were inconsistently reported across the decades covered, and standardized outcome measures were rarely available.

A further limitation concerns the geographic and demographic distribution of the reports included. The vast majority of cases originated from centers in Europe, North America, and East Asia, with a striking underrepresentation of African, Latin American, South Asian, and Middle Eastern populations. This unbalanced distribution likely reflects unequal access to tertiary HN oncology referral centers, advanced diagnostic facilities, and academic publishing platforms, rather than a genuine epidemiological pattern, and entails a substantial risk of ascertainment bias. In parallel, racial and ethnic demographics of the patients included were rarely reported. The absence of these data prevents any meaningful subgroup analysis and implies that conclusions on clinical presentation, treatment, and survival are based on a predominantly male, white, Western cohort. Future efforts should prioritize prospective, multicenter, international registries that systematically capture demographic, socioeconomic, racial, and ethnic data alongside oncological information, to provide more robust and equitable evidence on this rare clinical entity.

CONCLUSIONS

Despite its rarity, a laryngeal metastasis must be kept in mind whenever facing differential diagnosis of a laryngeal mass, especially in a patient with a known or suspected prior or

synchronous extralaryngeal malignancy, and particularly in patients with prostate, renal, colorectal, pulmonary, or skin (melanoma) primaries. Prompt endoscopic evaluation, cross-sectional imaging, and biopsy with tailored immunohistochemistry remain the cornerstones for adequate diagnosis. Management should be multidisciplinary and individualized, with an emphasis on airway-securing treatment, proactive control of symptoms, and, whenever possible, systemic therapy.

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Claudia Montenegro, Fatima Ezzarah Nassih, Cesare Piazza, and Alfio Ferlito collected data and performed analysis and interpretation of data and took part in drafting the article.

Cesare Piazza and Alfio Ferlito revised it critically for important intellectual content, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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Data Availability. Datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Conflict of Interest. Alfio Ferlito is an Editorial Board member of *Oncology and Therapy*. Alfio Ferlito was not involved in the selection of peer reviewers for the manuscript nor any of the subsequent editorial decisions. Claudia Montenegro, Cesare Piazza, and Fatima Ezzarah Nassih have nothing to disclose.

Ethical Approval. This article is based on previously conducted studies and does not contain any new studies with human participants or

animals performed by any of the authors. Institutional review board approval and informed consent were not required, in accordance with our institutional policy.

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