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# Ranula, Its Etiopathogenesis And Management; A Systematic Review

## Abstract

Ranula is defined as a swelling on the floor of the mouth, and its etiology is unclear. Aspects of etiopathogenesis, origin, and management remain debatable. The rationale of our study was to eliminate the discrepancies pertaining to the etiopathogenesis and management of ranula. Our objective was to determine the etiopathogenesis of ranula by systematically reviewing the available literature and to establish the best treatment protocol for ranula (intraoral and plunging). Case series, case reports, and observational and longitudinal studies referring to the etiology, pathogenesis, and management of ranula were included, and the previously published review articles were excluded from our study. We performed an electronic search from the year of inception of the database to December 2019. PubMed, Science direct, and Google Scholar databases were explored without restrictions of language or publication date. The search algorithm was Ranula {Mesh Major topic} and {Etiopathogenesis}, Ranula {Mesh Major topic} and {Management}. A total of 64 full-text articles were assessed. We concluded that the presence of the Bartholin duct might be a possible cause of intraoral ranula development, indicating that it originates from greater sublingual gland. Intraoral and plunging ranula are traumatic extravasation pseudocysts. Congenital ranula are histopathologically classified retention cysts lined with stratified squamous epithelium. The mylohyoid muscle exhibits dehiscence, which is commonly present in the anterior two-third part from which a part of the sublingual gland can be herniated or mucus can extravasate, leading to the formation of plunging ranula. Transoral excision with complete excision of ipsilateral sublingual gland remains the gold standard treatment of intraoral ranula and gold standard surgical treatment for plunging ranula. For mixed ranula, the treatment includes transoral excision of the sublingual gland along with the drainage of cyst.

**Keywords:** Bartholin's duct, greater sublingual gland, ranula, plunging ranula

## Introduction

The etiopathogenesis of ranula is not clearly defined, and the best possible method of ranula management is debatable. We conducted a detailed systematic review of the available literature to overcome this discrepancy.

### Rationale and Objectives

**Rationale:** to eliminate the discrepancies pertaining to the etiopathogenesis and management of ranula.

**Objective:** to determine the etiopathogenesis of ranula by conducting a systematic review of the available literature and to explore the best treatment protocol for ranula (intraoral and plunging) by reviewing the available literature.

## Methods

### Structured Questions

1. What is the etiopathogenesis of ranula formation and mechanism of plunging ranula?
2. What is the best possible management of ranula?

### Selection Criteria (for Articles)

All articles describing etiology, pathogenesis, and management of ranula were included. Case series, case reports, and observational studies and longitudinal studies referring to the above-mentioned topic were included. All previously published review articles were excluded.

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### Literature Search Strategy

An electronic search was performed from the year of inception of the database to December 2019. PubMed, Science direct, and Google Scholar databases were explored without language or publication date restrictions. The search algorithm was Ranula {MeSH Major topic}and {Etiopathogenesis}, Ranula {MeSH Major topic} and {Management}. Back referencing of the selected articles was performed, and the related article obtained therein was also added to the study.

### Data Collection and Analysis

The articles were evaluated for relevance to the research question based on their title and abstract. According to pretext eligibility criteria, significant articles were subjected to full-text evaluation, and subsequently, these were subjected to data extraction and data analysis.

## Results

Sixty-four full-text articles were assessed. These included case reports (n = 38), case series (n = 7), retrospective studies (n = 10), prospective studies (n = 9), articles focusing on simple intraoral ranula (n = 12), plunging ranula (n = 28), congenital ranula (n = 17), ranula (plunging or intraoral unspecified) (n = 3), cadaveric dissection studies (n = 4), articles focusing on etiopathogenesis (n = 43); articles describing the mechanism of plunging ranula (n = 11 [five radiological studies, two cadaveric dissections, and four surgical studies]). Articles focusing on the management of ranula were 38.

## Discussion

Since ancient times, several theories have been proposed regarding the origin and pathogenesis of ranula. The discrepancy in the gland of origin, pathogenesis of cyst formation, and the best strategy to manage cases with the development of minimum complications are reflected in the available literature. We have attempted to review the maximum possible literature to put forth explanations for the above-mentioned aspects.

### Role of The Greater Sublingual Salivary Gland, Bartholin Duct, and Ducts of Rivinus in Ranula Formation

Ducts of Rivinus are a group of excretory ducts draining the sublingual gland, and most ducts open into the floor of the mouth. The Bartholin duct is the largest of the sublingual excretory ducts, and it either joins Wharton's duct or opens independently into the floor of mouth. McMurrich[1] and Thoma[2] observed in their cadaveric studies that the sublingual gland consisted of greater sublingual gland, a constant segment with a separate duct known as the Bartholin duct (major sublingual duct), and a constant lesser sublingual gland consisting of numerous smaller glands, each presenting with separate duct openings into the floor of mouth. Around 1967, Lippi[3] in his cadaveric study stated that although it was difficult to present an accurate illustration, the adult human sublingual gland was composed of two components. The greater sublingual gland was intermediate in position between the lesser sublingual gland anterolaterally and main submandibular duct medially. The duct of the greater sublingual gland joined the terminal portion of the submandibular duct or opened independently. The lesser sublingual gland was always present and usually consisted of a triangular shaped mass of numerous small glands located in the anterior portion of paralingual space. More recently, McGurk et al.[4] in their observational study of oral ranula, which included 8 patients with transoral excision, reported that cell communication between the cyst and the sublingual salivary gland was observed in all patients, and the communication was achieved by a main duct that passed through the cyst. Mun et al.[5] in their prospective study of sublingual gland excision conducted to determine ductal variation of the sublingual gland as a predisposing factor for ranula formation reported that 88.9% of the oral ranula cases showed the presence and anatomic variation of the Bartholin duct; however, only three of the seven patients with plunging ranula showed this variation, whereas the 11 control patients (undergoing sublingual gland excision for other reasons) did not show variation in the Bartholin duct. A study conducted by Zhang et al.[6] to determine whether patients with anatomic variation of sublingual or Wharton ducts were predisposed to ranula formation reported that 32 of the 55 patients with ranula and 1 of the 15 patients without ranula had variation in the Bartholin duct.

### Ranula: An Extravasation or Retension Cyst?

Rayne[7] (one patient), de Visscher[8] (four patients), Olasoji et al.[9] (two patients), Pandit et al.[10] (six patients), Hidaka et al.[11] (two patients), Ghani et al.[12] (eight patients), Arunachalam[13] (two patients), Samant et al.[14] (95 patients), Suresh[15] (one patient), Mustafa et al.[16] (one patient), Kim et al. [17] (one patient), McKinstry et al.[18] (two patients), Olojede et al.[19] (four patients), and Kamlakaran et al.[20] (one patient) in their studies of plunging ranula described the histopathology as extravasation pseudocyst, that is, chronic inflammatory wall lined with dense fibrous connective tissue with macrophages. The epithelial lining of the salivary duct system may or may not be associated, and normal mucous acini may be observed. Yuca et al.[21] (nine patients), McGurk et al.[4] (eight patients), Ghani et al.[12] (six patients), and Date et al.[22] (one patient) have reported cases of intraoral ranula that were not congenital, and elucidated the extravasation mechanism for ranula development.

Etiology for extravasation is mostly ascribed to trauma. Trauma causes damage of sublingual gland acini and results in ductal obstruction. Blockage of the sublingual ducts in turn leads to increase in hydrostatic pressure causing extravasation of mucus into surrounding sub-mucosa and finally leads to pseudocyst formation.[23] McGurk et al.[4] stated that histologic examination of the ranulas showed the presence of cystic extravasation mucoceles in all cases. They further stated that the findings in their study supported traumatic etiology in most ranula cases. Harrison et al.[24] in their cadaveric dissection study explained that oral ranulas were extravasation mucoceles that usually arose after the occurrence of the trauma of the duct of Rivinus of one of the masses of small salivary glands that constituted the lesser sublingual gland. Extravasated mucus from the torn duct of Rivinus could pass through the mylohyoid hiatus as well as through the posterior part of the mylohyoid muscle to form a plunging ranula. However, the sublingual gland herniated through the mylohyoid hiatus could be subjected to trauma and undergo rupture, which could lead to the extravasation of mucus and the direct formation of a plunging ranula. Additionally, obstruction of a herniated sublingual gland may lead to acinar rupture and extravasation of mucus.

Congenital ranula is a type of retention cyst and is intraoral as reported by Redpath et al.[25], Hoggins et al.[26], Pownell et al. [27], Fer-

nandez et al.[28], Ugboko et al. [29], Onderoglu et al.[30], Kolker et al. [31], Cavalante et al.[32], Marques et al.[33], Soni et al.[34], Singh et al.[35], Mneimneh et al.[36], Pant et al.[37] in their case reports of a single patient. They all described the histopathology as a simple cyst lined with stratified squamous epithelium with the presence of mucous gland within the cyst wall. Redpath et al. reported congenital atresia of the submandibular gland as the etiology; and Hoggins et al.[26] and Pownell et al.[27] have reported the existence of imperforate submandibular salivary ducts in their case reports.

### Plunging Ranula: Mylohyoid Dehiscence and Herniation of the Sublingual Gland

Morestein[38] discovered the mylohyoid hiatus and found up to three hiatuses in one cadaver, although he reported the glandular prolongation through mylohyoid as the sublingual gland, which explained the plunging ranula. Gaughran et al.[39] conducted a study based on the cadaveric dissection of 324 cadavers and stated that 117 cadavers were found to contain one or more distinct masses of tissue resting on the inferior surface of the mylohyoid muscle, and 102 cadavers were found to contain the sublingual gland in the inframyloid processes. Engel et al.[40] conducted a cadaveric study of sixty-three herniations and reported that thirty were associated with the sublingual gland, twenty-eight were associated with the submandibular region, four were associated with the adipose tissue, and one was associated with cholesteatoma. Harrison et al.[24] conducted a cadaveric study of 23 cadavers and reported that mylohyoid hiatus was found in 10 (43%) of the 23 cadavers and that the hernia protruded through every hiatus; furthermore, there were a total of 15 hiatuses. They further stated that the sublingual gland was identified in nine hernia cases, and the submandibular gland was not present. The remaining six hernias consisted of fat.

Jain et al.[41], Jain and Jain[42], Samant et al.[14], and Lee et al.[43] in their radiological studies of plunging ranula reported the continuity of the sublingual gland via the mylohyoid hiatuses. Jain et al[41] used ultrasonography and reported mylohyoid defects in 100% of their cases (33 patients). Samant et al.[14] used both computed tomography (CT) and real time ultrasonography and stated that virtually all radiology reports described the existence of a defect in the mylohyoid. There was evidence of herniation of the sublingual gland in 27 patients with real-time herniation on movement of the sublingual gland, based on movement of the tongue from side to side which was observed with the performance of ultrasound in 25 patients. Jain and Jain[42] performed an ultrasonographic study of 76 patients with 80 plunging ranulas and showed the association of the sublingual gland through mylohyoid defects. They reported mylohyoid defects in 98% of their patients, and sublingual gland herniation was present in 76 of the 80 plunging ranula. Lee et al.[43] in their retrospective study of 41 patients with plunging ranula using CT scan (post contrast axial and direct or reformatted coronal) reported the presence of mylohyoid dehiscence in 36 patients, 30 of whom had sublingual gland herniation.

Scheinder et al.[44], Rayne[7], Braun et al.[45], and Takimoto et al.[46] in their case reports of single cases of plunging ranula performed surgery and observed the presence of the sublingual gland as a herniated mass from mylohyoid dehiscence. Ichimura et al.[47] in their case series of 7 plunging ranula reported dehiscence in 2 patients and plunging via posterior route in the remaining patients during surgical removal. Mortan et al.[48] in their series of 80 plunging ranula conducted surgery and proved mylohyoid dehiscence in 67 of the 80 cases.

Mylohyoid dehiscence is located in the anterior third part as reported by Gaughran[39] and Harrison et al.[24] in their cadaveric study, and this has been also reported by Jain and Jain[44] and Lee et al. in their radiological studies. The posterior route of the entry of ranula was reported by Ichimura[47] (surgically). Kuryabayashi et al. [49] performed MRI for 12 patients of plunging ranula, and Li and Li[50] used MRI for three patients. Lee et al.[43] conducted CT scans and found a posterior route of entry, which is also known as the classic tail sign, in 5 of the 41 patients.

## Management of Ranula

### Intraoral Ranula

### Wait-and-Watch Policy and Aspiration

Steelman et al.[51] and Bernhard et al.[52] have stated that congenital intraoral ranula has a tendency to resolve spontaneously, without recurrence; hence observation for spontaneous resolution is recommended for a period of 1 year in uncomplicated cases. Aspiration of the cyst was performed by Zhi et al.[53] for 2 out of the 11 pediatric patients with intraoral ranula with no recurrence in both patients. Soni et al.[34] aspirated a congenital ranula in their patient without any reported recurrence.

### Marsupialization and Micro-Marsupialization

Marsupialization is a relatively coarse minimally invasive procedure where the bottom of the ranula cavity and oral mucosa are subjected to treatment to establish continuity by removing the cyst wall and by suturing the boundary of the cyst with oral mucosa. Yuca et al.[21] (nine pediatric patients) and Bonet et al.[54] (52 pediatric ranulas) used marsupialization as treatment without any recurrence. Cavalante et al.[32] performed marsupialization for congenital ranula with no recurrence. Micro-marsupialization for treatment of ranula was first mentioned by Mortan and Bartley[55]. It is a procedure performed under local anesthesia administered for 3 minutes, and thereafter, silk sutures are passed through the internal part of the lesion along its widest axis, and finally a surgical knot is placed. The sutures are removed after a week. Delhem et al.[56], Sandirini et al.[57], and Raj et al.[58] have mentioned the use of micro-marsupialization for oral ranula in pediatric patients. A recurrence rate as high as 66.67% for marsupialization was reported by Zhao et al.[59] in their retrospective study of complications associated with surgical management of ranula (606 procedures, 571 patients). Recurrence with micro-marsupialization was 10%-43%.[56,57,58]

### Sclerotherapy

Picnibil OK432, a lyophilized mixture of low virulence strain of Streptococcus pyogenes incubated with benzylpenicillin, was first introduced for treatment of lymphangiomas, and its use was further extended to ranula. Watanabe et al. [60] (case report, one adult patient), Lee et al.[61] (retrospective study of 13 pediatric patients), and Yoshizama et al.[62] have used OK432 intralesionally without any reported recurrence. Nickel gluconate-mercurius heel-potentized swine organ preparation as a homotoxicological therapy was performed by Garofalo et al.[63] in nine pediatric patients for intraoral ranula with the achievement of complete response in eight of them.

### Transoral Excision of Ranula and Sublingual Gland

Pandit et al.[10] in their case series of six intraoral ranulas reported that transoral excision of the ranula and the offending sublingual gland was performed in four patients without any recurrence. McGurk et al.[4] in their prospective study of eight adult patients with oral ranula also conducted transoral excision of ranula along with the sublingual gland with no recurrence reported in a mean 26-month follow-up period. Shehata et al.[64] conducted a prospective randomized control trial to compare the results of marsupialization and sublingual sialoadenectomy for pediatric intraoral ranula involving 24 patients and concluded that recurrence was found to be more with marsupialization (41.6%), whereas infection and transient lingual nerve paresis might be associated with sublingual sialoadenectomy. Zhao et al.[59] have reported only 1.5% recurrence with the excision of ranula and the sublingual gland.

### Plunging Ranula

### Sclerotherapy

Fukase et al. [65] used of OK432 for 11 patients with plunging ranula, but only five cases showed complete resolution with a single injection. Rho et al.[66] conducted ultrasound-guided transcervical intracystic Picnibil in 21 patients with plunging ranula and reported that total shrinkage without recurrence was noted in 7 (33%) patients. Recurrence after last injection (mean: 1.7 injections) was observed in 3 (14.3%) patients after the occurrence of total and near total shrinkage. They reported an overall recurrence rate of 47% after each injection. Percutaneous ethanol ablation was performed by Ryu et al.[67] in their retrospective study, and this resulted in the complete resolution of ranula in nine patients and incomplete response in 11.

### Transoral Excision of the Sublingual Gland with Ranula Evacuation

Transoral excision of the sublingual gland along with ranula evacuation was reported by de Visscher et al. [8] and Li et al.[50] in their case series of four and three patients, respectively, and by Olasoji et al.[9], Hidaka et al. [11], Arunachalam et al.[13], Mustafa et al.[16], and Kim et al.[17] in their case reports. Huang et al.[68] in their retrospective study involving 18 patients have reported a success rate of 94.4% and transient lingual nerve paresthesis in 11.1% of the patients. Mortan et al. [48] in a retrospective study reported that of the 69 patients who underwent surgery, three experienced recurrence, three presented with submandibular swelling, and one developed an infection. Samant et al.[14] in their prospective follow-up study of 81 patients concluded that simple transoral sublingual gland excision with evacuation (but not excision) of the cervical cystic content provided excellent results. Complications were reported as four patients presented with postsurgical infection, two experienced trauma to the submandibular duct leading to submandibular gland excision later, and seven patients presented with transient lingual nerve paresthesia. Zhao et al.[59] in their retrospective study of the complications associated with surgical management of ranula have reported that 356 patients underwent excision of the sublingual gland of which only 286 were subjected to follow-up for more than six months; furthermore, recurrence was reported in 3 of the 286 cases and numbness of tongue was reported in 6 of the 286 cases. Their study did not differentiate between the types of ranula.

### Transcervical Ranula Excision with Sublingual Gland Excision

Ichimura et al.[47] in their review involving cases of seven patients emphasized the excision of the sublingual gland along with the excision of ranula in all their patients using a transcervical approach, though they reported transient palsy of the marginal mandibular nerve in four of the seven patients. Olejede et al.[19] and Kamlakaran et al.[20] have mentioned sublingual gland excision with ranula excision in their case reports. No recurrence was reported in any patient during the conduction of follow-up. Zhao et al.[59] have reported 213 excision cases of both the sublingual gland and ranula and 28 excision cases pertaining to ranula only. They also reported that most complications were related to the excision of the gland and ranula.

## Conclusion

We conclude that the sublingual gland has a constant lesser lobe and a variant greater lobe. The lesser lobe drains through numerous ducts into the floor of the mouth. The greater lobe drains through a separate Bartholin duct, which joins the terminal portion of submandibular duct or opens independently. The presence of the Bartholin duct may be a possible cause of intraoral ranula development, indicating that ranulas originate from the greater sublingual gland.

Intraoral and plunging ranula are trauma-associated extravasation pseudocysts. Congenital ranula are histopathologically classified retention cysts lined by stratified squamous epithelium.

The mylohyoid muscle exhibits dehiscence, which is commonly present in the anterior two-third part of the muscle, through which a part of the sublingual gland herniates. Extravasated mucus from the sublingual gland can pass through the mylohyoid hiatus into neck or can trickle down from the posterior free border of the mylohyoid muscle, leading to the formation of plunging ranula.

An effective method of treatment for pediatric intraoral ranula cannot be formulated. Large, well-designed studies for OK432 and homotoxicological drugs were unavailable in the literature. A wait-and-watch policy for smaller intraoral ranula and marsupialization or excision of sublingual gland cysts are surgical options for pediatric intraoral ranulas >2 cm.

For adult intraoral ranulas, marsupialization with or without gauze packing, excision of ranula with total excision of the sublingual gland, or ranula excision with partial excision of the sublingual gland are surgical treatment options. Although marsupialization has a high recurrence rate, gauze packing reduces the rate of recurrence. However, only case reports and low case series are available in the literature in favor of gauze packing.

Excision of ranula with partial sublingual gland excision is based on cadaveric and surgical finding of the Bartholin duct and greater sublingual gland and its association with oral ranula. This procedure can be performed for small ranula, where a surgeon can trace the origin of ranula from the segment of the sublingual gland through meticulous dissection. This conservative treatment warrants larger multicenter studies for substantiation. Transoral excision of ranula with complete excision of ipsilateral sublingual gland remains the gold standard treatment for intraoral ranula.

The gold standard surgical treatment for plunging ranula and mixed plunging-sublingual ranula involves the transoral excision of the sublingual gland along with the drainage of pseudocyst contents.

Many authors suggest the adoption of a transcervical approach for plunging ranula (without intraoral component). Studies have reported the complete excision of the cyst and removal of the sublingual gland by retracting mylohyoid superiorly. Removal of the submandibular gland facilitates exposure. Morbidity in the transcervical approach is considerably higher than the transoral approach in terms of incision, drainage, and marginal mandibular nerve palsy. The transcervical approach can be used as salvage surgery for recurrence after transoral excision of the sublingual gland and the drainage of cyst contents.

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