



MASCC/ISOO Clinical Practice Statement: Clinical assessment of salivary gland hypofunction and xerostomia in cancer patients

Catherine Hong¹ · Joel B. Epstein^{2,3} · Siri Beier Jensen⁴ · Luiz Alcino Gueiros⁵ · Stephanie J. M. van Leeuwen⁶ · Abhishek Kandwal⁷ · Arjan Vissink⁸ · Sharon Elad⁹

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Abstract

Purpose A MASCC/ISOO Clinical Practice Statement (CPS) is aimed at generating a concise tool for clinicians that concentrates practical information needed for the management of oral complications of cancer patients. This CPS is focused on the clinical assessment of salivary gland hypofunction and xerostomia in cancer patients.

Methods This CPS was developed based on a critical evaluation of the literature followed by a structured discussion of a group of leading experts, members of the Oral Care Study Group of MASCC/ISOO. The information is presented in the form of succinct bullets and tables to generate a short manual about the best standard of care.

Results The objective assessment of saliva secretion involves an extra- and intra-oral clinical examination while the subjective assessment involves eliciting information on the patient's complaint of xerostomia and its impact on daily functioning. This CPS summarizes the common investigator- and patient-reported instruments used in clinical practice for assessing salivary gland hypofunction and xerostomia in cancer patients.

Conclusion There is a range of tools to assess salivary gland function in patients undergoing cancer therapy, patients recovering from cancer therapy, or cancer survivors. Clinicians should ideally conduct both objective and subjective measurements to ensure a clear understanding about the status of the patients in order to provide the most appropriate treatment.

Keywords Cancer · Dry mouth · Xerostomia · Salivary gland hypofunction · Oral manifestations

✉ Catherine Hong
denchhl@nus.edu.sg

Joel B. Epstein
jepstein@coh.org

Siri Beier Jensen
siri@dent.au.dk

Luiz Alcino Gueiros
luiz.mgueiros@ufpe.br

Stephanie J. M. van Leeuwen
Stephanie.vanLeeuwen@radboudumc.nl

Abhishek Kandwal
way2drabhi@gmail.com

Arjan Vissink
a.vissink@umcg.nl

Sharon Elad
SElad@URMC.Rochester.edu

² Dental Oncology Services, City of Hope Duarte, Duarte, CA, USA

³ Cedars-Sinai Health System, Los Angeles, CA, USA

⁴ Department of Dentistry and Oral Health, Aarhus University, Aarhus, Denmark

⁵ Department of Clinic and Preventive Dentistry, Federal University of Pernambuco, Recife, Pernambuco, Brazil

⁶ Department of Dentistry, Radboud university medical center, Nijmegen, The Netherlands

⁷ Cancer Research Institute, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Dehradun, Uttarakhand, India

⁸ Department of Oral and Maxillofacial Surgery, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands

⁹ Oral Medicine, Eastman Institute for Oral Health, University of Rochester Medical Center, Rochester, NY, USA

¹ Discipline of Orthodontics and Paediatric Dentistry, Faculty of Dentistry, National University of Singapore, 9 Lower Kent Ridge Road, Singapore 119085, Singapore

Introduction

Salivary gland hypofunction and xerostomia in cancer patients may arise from the anti-neoplastic treatment itself, such as from head and neck radiotherapy, chemotherapy, radioiodine treatment, and immunotherapy, or as a manifestation of graft-versus-host disease in hematopoietic stem cell transplant recipients. Furthermore, polyparmacy is common in cancer patients. Many are on drugs with anti-cholinergic effects or opioids, which aggravate dry mouth [1].

The prevalence, severity, and duration of salivary gland hypofunction or xerostomia range considerably and depend on the type of anti-neoplastic treatment and the temporal relationship to the treatment [2, 3]. Salivary gland hypofunction may be life-long in cancer survivors who are post high-dose head and neck radiotherapy.

The Oral Care Study Group (OCSG) of the Multinational Association of Supportive Care in Cancer (MASCC) and the International Society of Oral Oncology (ISOO) have published several systematic reviews on salivary gland hypofunction and xerostomia in cancer patients [3, 4]. These reviews focused on the preventive and treatment recommendations. As qualitative and quantitative assessments of salivary gland hypofunction and xerostomia are integral to direct management strategies, a working group of the OCSG of MASCC/ISOO was established to formulate an expert opinion Clinical Practice Statement (CPS) to provide a summary of the clinical instruments for assessing salivary gland hypofunction and xerostomia in cancer patients.

Objective

The objective of this CPS is to provide clinicians with the common instruments used in clinical practice to assess salivary gland hypofunction and xerostomia in cancer patients.

Methods

This CPS was developed based on a critical evaluation of literature and discussion by experts in the field and the international working group of the OCSG of MASCC/ISOO. The CPS was further reviewed and approved by two independent boards: the ISOO Advisory Board and the MASCC Guidelines Committee.

Clinical assessment instruments

- The terms salivary gland hypofunction and xerostomia describe objectively low saliva secretion and

the subjective sensation of oral dryness, respectively. The term hyposalivation has been used in the literature to refer to the low end of salivary gland hypofunction.

- The objective assessment (Table 1) of saliva secretion involves an extra- and intra-oral clinical examination which should include the following:
 - Evaluation of the salivary glands
 - Assessment of saliva quantity and quality
 - Inspection of the oral mucosa and the dentition
- The subjective assessment elicits information on the patient's complaint of xerostomia (e.g., presence, severity, frequency, duration, diurnal fluctuation) and its impact on daily functioning (e.g., physical, social, psychological, oral function, quality of life).
 - These symptoms can be elicited with a single question or the use of an instrument specifically developed to assess xerostomia. The responses are often in binary response (i.e., presence/absence), a visual analogue scale, a numerical rating scale, or a 3/4/5-point Likert scale.
 - Table 2 details the common instruments that have been used to assess xerostomia in cancer patients. Subjective instruments that have been used in non-cancer patients are found in online Table 1.
 - Other symptoms that may be related to salivary gland hypofunction include a burning sensation, altered taste sensation, and mucosal sensitivity to intense flavors. If dental caries is present, the patient may have sensitivity to sweet foods.
- Table 3 lists the standard investigator-reported instruments used for assessing salivary gland hypofunction and/or xerostomia in cancer patients. These instruments are routinely used in specialized clinics (e.g., oncology, oral medicine) or for research purposes and often comprise of a composite of objective and subjective measurements, including quality of life assessment. Details of less commonly used investigator-reported instruments are found in online Table 2.
- There are several quality of life instruments, which include question/s eliciting the impact of salivary gland hypofunction or xerostomia on a patient's daily life [5]. The common instruments used in cancer patients are the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaires (QLQ) (e.g., EORTC QLQ-Oral Health 15, EORTC QLQ-Head & Neck43), Functional Assessment of Cancer Therapy

Table 1 Common objective clinical measures for salivary gland hypofunction

Objective measure	Procedure	Abnormal finding/s
Saliva quantity (sialometry)	<p>Unstimulated whole saliva flow rate (UWSR)^a</p> <ul style="list-style-type: none"> • Patient should be instructed to avoid eating, drinking, smoking, and toothbrushing 1 h before the procedure • Common collection methods: draining^b and spitting^c methods • Collection duration: 5, 10, or 15 min <p>Stimulated whole saliva flow rate (SWSR)^a</p> <ul style="list-style-type: none"> • Collection methods and duration as above with the addition of having the patient chew salivary stimulants • Common stimulants: standardize piece of paraffin wax, paraffin film, or sugar-free gum (1–2 g), 2% citric acid tongue application every 30 s throughout the collection duration 	<ul style="list-style-type: none"> • Salivary gland hypofunction <ul style="list-style-type: none"> - UWSR: ≤ 0.2 ml/min • Salivary gland hyposalivation <ul style="list-style-type: none"> - UWSR: ≤ 0.1 ml/min • Salivary gland hyposalivation <ul style="list-style-type: none"> - SWSR: ≤ 0.5–0.7 ml/min
Oral findings	<p>Clinical examination</p> <ul style="list-style-type: none"> • Mucosal and lip appearances • Saliva appearance • Oral clearance • Caries status • Salivary gland presentation • Opportunistic infections 	<p>These findings are not necessarily pathognomonic. Patients with salivary gland hypofunction often present with at least one of the below findings.</p> <ul style="list-style-type: none"> • Glassy appearance of oral mucosa • Mirror sticks to buccal mucosa or tongue • Altered gingival architecture (e.g., smooth) • Loss of tongue papillae • Dry and cracked lips • No saliva pooling in the floor of the mouth • Thick, sticky, frothy saliva • Mucoid strings of saliva on self-cleansing surfaces • Presence of food debris in usually self-cleansing areas • Root, incisal, and cervical rampant caries resulting in chipped incisal edges and coronal structure fractures • Demineralization of teeth • Denture surface is dry • Increased frequency of oral candidiasis • Increase frequency for retrograde sialadenitis (may be accompanied by redness, tenderness, and warmth on palpation of the salivary gland)
Others	<p>These other tests may be performed to assess salivary gland structure or function.</p> <ul style="list-style-type: none"> • Sialography (e.g., radiosialography, computed tomography sialography, cone beam computed tomography sialography, magnetic resonance imaging sialography) • Scintigraphy • Sialoendoscopy • Salivary gland ultrasound • Saliva analysis (e.g., pH, biochemistry, physical properties tests) • Modified Schirmer test [6] 	

^aUnstimulated and stimulated saliva flow rate may be measured from the individual glands (e.g., parotid gland, submandibular glands), but these are primarily performed in specialized salivary gland disorder clinics or for research purposes

^bDraining method: The patient is instructed to swallow and then to tilt the head forward so that saliva flows anteriorly in the mouth. After the initial swallow, the patient allows saliva to drain continuously from the lower lip through a funnel into a graduated cylinder for a specified duration, at the end of which residual saliva in the mouth is spat out

^cSpitting method: Saliva is allowed to accumulate in the floor of the mouth with the mouth closed. The patient spits the saliva out into a test tube every 60 s, whenever they experience the urge to swallow the accumulated fluid or when the patient feels the accumulation of saliva naturally. The tube can be fitted with a funnel to ease collection of saliva

(FACT) Questionnaires (e.g., FACT-Head & Neck), MD Anderson Symptom Inventory, Memorial Symptom Assessment Scale, Patient Reported Outcomes–Common Terminology Criteria for Adverse Events, Rotterdam Symptom Checklist, University of Washington Quality of Life Questionnaire, and Vanderbilt Head and Neck Symptom Survey.

Practical considerations

- The correlation between salivary gland hypofunction and xerostomia is poor. Therefore, not all patients with xerostomia demonstrate the clinical signs and symptoms of salivary gland hypofunction and vice versa. Thus, clinicians should ideally perform objective and subjective

Table 2 Common subjective (patient-reported) clinical instruments for assessing xerostomia in cancer patients

Subjective measure	Question/s and format of response/s
1. Visual Analogue Scale or Numerical Rating Scale	<ul style="list-style-type: none"> ● 0–100 mm or 0–10 cm ● 0–10 step
2. Xerostomia Inventory [7, 8]	<p>Rated on a 5-point Likert scale (1. Never; 2. Hardly ever; 3. Occasionally; 4. Fairly often; 5. Very often)</p> <ol style="list-style-type: none"> 1. I sip liquids to help swallow food 2. My mouth feels dry when eating a meal 3. I get up at night to drink 4. My mouth feels dry 5. I have difficulty in eating dry foods 6. I suck sweets or cough lozenges to relieve dry mouth 7. I have difficulties swallowing certain foods 8. The skin of my face feels dry 9. My eyes feel dry 10. My lips feel dry 11. The inside of my nose feels dry <p>The questions #2, 4, 5, 7, and 10 comprise the summated Xerostomia Inventory-Dutch Version rated on a 3-point Likert scale (1. Never; 2. Occasionally; 5. Often).</p>
3. Xerostomia Questionnaire [9]	<p>Rated on an 11-point Likert scale (0–10; the higher the score, the worse the xerostomia)</p> <ol style="list-style-type: none"> 1. Rate your difficulty in talking due to dryness 2. Rate your difficulty in chewing due to dryness 3. Rate your difficulty in swallowing solid food due to dryness 4. Rate the frequency of your sleeping problems due to dryness 5. Rate your mouth or throat dryness when eating food 6. Rate your mouth or throat dryness while not eating 7. Rate the frequency of sipping liquids to aid swallowing food 8. Rate the frequency of sipping liquids for oral comfort when not eating
4. Groningen Radiotherapy-Induced Xerostomia Questionnaire [10]	<p>Rated on a 4-point Likert scale (Not at all; A little; Quite a bit; Very much (then converted to 0–100 scale))</p> <ol style="list-style-type: none"> 1. Have you had a dry mouth during the day? 2. Have you had a dry mouth outdoors? 3. Have you had difficulties with eating due to a dry mouth? 4. Have you had a dry mouth during activities? 5. Have you had difficulties with talking due to a dry mouth? 6. Did you drink more during the day due to a dry mouth? 7. Have you had a dry mouth during the night? 8. Have you had difficulties with sleeping due to a dry mouth? 9. Did you need to drink during the night due to a dry mouth? 10. Have you had sticky saliva during the day? 11. Have you had difficulties with eating due to sticky saliva? 12. Have you had difficulties with talking due to sticky saliva? 13. Have you had sticky saliva during the night? 14. Have you had difficulties with sleeping due to sticky saliva?
5. Xerostomia Quality of Life Scale [11]	<p>Rated on a 5-point Likert scale (Not at all; A little; Somewhat; Quite a bit; Very much)</p> <ol style="list-style-type: none"> 1. My mouth/throat dryness limits the kinds or amounts of food I eat 2. My mouth/throat dryness causes discomfort 3. My mouth/throat dryness causes a lot of worry or concern 4. My mouth/throat dryness keeps me from socializing (going out) 5. My mouth/throat dryness makes me uncomfortable when eating in front of other people 6. My mouth/throat dryness makes me uncomfortable speaking in front of other people 7. My mouth/throat dryness makes me nervous 8. My mouth/throat dryness makes me concerned about the looks of my teeth and mouth 9. My mouth/throat dryness keeps me from enjoying life 10. My mouth/throat dryness interferes with my daily activities 11. My mouth/throat dryness interferes with my intimate relationships 12. My mouth/throat dryness has a bad effect on tasting food 13. My mouth/throat dryness reduces my general happiness with life 14. My mouth/throat dryness affects all aspects of my life 15. If you were to spend the rest of your life with your mouth/throat dryness just the way it is now, how would you feel about this? Delighted; Mostly satisfied; Mixed: equally satisfied/dissatisfied; Mostly dissatisfied; Terrible

Table 2 (continued)

Subjective measure	Question/s and format of response/s
6. Amosson et al. [12]	Rated on a mix of 3- or 4-point Likert scale and dichotomized responses 1. What is the overall comfort of the mouth? Very comfortable/Slight dryness/Moderate dryness/Significant dryness 2. Does your mouth feel dry when eating? No/Mild/Moderate/Severe 3. Do you have difficulty swallowing any foods? Yes/No 4. Do you need to sip liquids to swallow dry food? Yes/No 5. Do you feel thirsty all the time? Yes/No 6. Do you feel that the amount of saliva in your mouth is... Too little/Adequate/Too much 7. Do you have problems with speech because of dry mouth? Yes/No 8. Does dry mouth interfere with your ability to sleep all the time? No/Occasionally/Frequently 9. Has your taste changed due to salivary gland function? Yes/No 10. Do you need to carry a water bottle daily? No/Occasionally/Frequently/All the time

Table 3 Common investigator-reported clinical instruments for assessing salivary gland hypofunction and xerostomia in cancer patients

Instrument	Grade
National Cancer Institute CTCAE Version 5	Grade 1—symptomatic (e.g., dry or thick saliva) without significant dietary alteration; unstimulated saliva flow > 0.2 ml/min Grade 2—moderate symptoms; oral intake alterations (e.g., copious water, other lubricants, diet limited to purees and/or soft, moist foods); unstimulated saliva 0.1 to 0.2 ml/min Grade 3—inability to adequately aliment orally; tube feeding or total parenteral nutrition indicated; unstimulated saliva < 0.1 ml/min
Toxicity criteria of the RTOG/EORTC	Acute Grade 0—no change over baseline Grade 1—mild mouth dryness, slightly thickened saliva, slightly altered taste such as metallic taste, alteration in baseline feeding behavior such as increased use of liquids with meals Late Grade 0—none Grade 1—slight dryness of the mouth; good response on stimulation Grade 2—moderate dryness of the mouth; poor response on stimulation Grade 3—complete dryness of the mouth; no response on stimulation
LENT-SOMA	Grade 1—normal moisture Grade 2—scant saliva Grade 3—absence of moisture; sticky, viscous saliva Grade 4—absence of moisture; coated mucosa

CTCAE Common Terminology Criteria for Adverse Events, RTOG/EORTC Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer, LENT-SOMA Late Effects Normal Tissue Task Force-Subjective, Objective, Management, Analytic

measurements to ensure that all patients reporting of xerostomia or presenting with an objective finding of salivary gland hypofunction are provided with appropriate management.

- Using a consistent set of instruments and possibly repeating these measurements to evaluate temporal changes in signs and symptoms are ideal. That means to perform the measurement each visit at the same time of the day.
- Clinicians should be mindful that salivary gland hypofunction and xerostomia are affected by several factors (e.g., patient's emotional state, fluid intake, medications, temporal relationship to cancer therapy). Thus, if appropriate, repeated measurements on different days to confirm findings of salivary gland hypofunction or xerostomia may be required.

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Declarations

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