紅唇族鼻塞流鼻水 確診口腔癌

記者顏宏駿／彰化報導

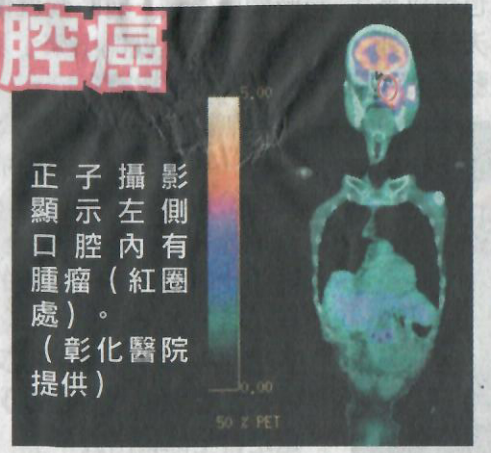
53歲的鍾先生長期鼻塞、流鼻水，原以為是鼻竇炎、鼻息肉作怪，長期吃藥配合鼻噴劑均未能改善，直到連呼吸和說話都感到困難，改到衛福部彰化醫院就醫。醫師發現他的問題不在鼻子，而是口腔癌的腫瘤往上侵犯鼻竇腔，造成鼻子症狀。

鍾先生鼻塞、流鼻水的症狀已近一年，先到耳鼻喉科診所就診，長期吃藥皆未見效果，他一直以為罹患鼻竇炎，用鼻噴劑可獲得鼻子短暫通暢，但鼻塞的情況越來越嚴重，最近連呼吸和說話都感到吃力，於是轉往彰化醫院就診。

彰化醫院耳鼻喉科主任許嘉方表示，鍾先生來診時常要用嘴巴呼吸，說話會「大舌頭」，這種發音障礙是鼻塞引起，雖然鍾先生一口咬定是鼻竇炎引起，但他發現鍾先生吃檳榔已有30年，真正的病灶恐怕不單純在鼻子。

4公分腫瘤竄向鼻竇腔

許嘉方說，經過電腦斷層及病理切片、正子攝影等檢查，發現鍾先生的左側牙齦內有一個約4公分的惡性腫瘤，往上穿越骨頭，破壞到鼻竇腔，引起鼻子適；目前鍾先生正接受放射線治療和化學治療，鼻子的症狀改善很多。



正子攝影顯示左側口腔內有腫瘤（紅圈處）。（彰化醫院提供）

鍾先生左邊鼻塞特別嚴重，沒想到竟是口腔癌引起。（彰化醫院提供）

許嘉方表示，研究顯示，口腔癌主要成因是口腔受到長期慢性的刺激，嚼檳榔、吸菸、喝酒、尖銳的蛀牙或不當假牙等都是原因，其中約9成的口腔癌患者都有嚼檳榔的習慣；另外，嚼食檳榔、吸菸及喝酒皆有者，罹患口腔癌的機率為一般人高出許多，從各方面的研究及報告來看，嚼檳榔和口腔癌的關係密不可分。

里長拔腳趾甲 張嘴大叫
醫師驚見口腔腫塊

許姓里長以過來人的經驗，奉勸大家不要再抽菸及吃檳榔。（記者湯世名攝）

記者湯世名／彰化報導

44歲彰化縣鹿港鎮街尾許姓里長，因工作關係常吃檳榔提神，幾乎每天要吃上百顆，一吃就是24年，甚至自己開起檳榔攤；而他對口腔出現不明病灶不以為意，直到前年就醫拔除腳趾甲，因疼痛張嘴大叫，被眼尖的醫生發現口腔內有腫塊，確診罹患早期口腔癌，幸好發現得早，手術切除腫塊，嚇得他發誓「再也不敢吃檳榔了」！

罹患早期口腔癌

彰化基督教醫院院長陳穆寬說，口腔癌是台灣青壯年男性最常見癌症，其中30至64歲中壯年發生人數高達7成，原因與抽菸及台灣特有的檳榔文化脫不了關係。嚼食檳榔不但會造成口腔黏膜病變，也可能導致癌癥。目前政府提出免費四癌篩檢，「口腔黏膜篩檢」最簡單快速，就可得知是否有口腔癌。

他指出，口腔癌早期病灶包括口腔白斑、口腔紅斑、潰瘍及口腔黏膜下纖維化等癥狀，臨床上癥狀不明顯常被病患忽視，等到腫瘤愈來愈大才求診，往往都是第4期了。但早期口腔癌不僅治癒率高，且不會造成臉部外觀變形，因此18歲以上曾吃過檳榔的原住民、或30歲以上有抽菸或曾吃過檳榔的民眾，只要把握定期2年一次免費的口腔癌檢查，就能早期發現早期治療。

發誓再也不吃檳榔

許姓里長指出，2019年開刀以前，檳榔從早吃到晚，每天要吃上百顆，但因為這突如其來的癌症，讓他決心要戒除檳榔。

衛福部最新統計顯示，10大癌症發生率口腔癌排行男性癌症第4名，2018年有超過7000名男性罹患口腔癌，2019年逾3000名男性死於口腔癌，男性口腔癌發生率為女性的10.7倍，而研究顯示嚼檳榔者罹癌機率為一般人的28倍，同時有檳榔、菸、酒習慣者更高達123倍；定期接受口腔黏膜檢查，可降低有嚼檳榔或吸菸習慣的男性26%死亡風險。

健康充電站

中醫養生講座

中國醫藥大學附設醫院台北分院中醫科醫師曾偉哲，5月19日下午5時至6時，在該院一樓大廳院徽前衛教區（台北市內湖區內湖路二段360號）主講「中醫養生」。

洽詢電話為（02）2791-9696轉1008。

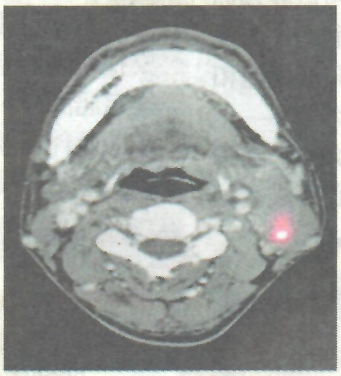
四期口咽癌難開刀 客製精準放療滅腫瘤

記者王俊忠／台南報導

43歲林姓男子有20餘年菸、酒史，7月因口腔有異物感、舌頭活動異常與左側頸部有腫塊而就醫，被診斷是第4期口咽癌，醫師對開刀手術沒把握，林男夫妻再求診台南市立安南醫院，醫師梁永昌為患者執行客製化的精準放射及化學治療，治療後1個月再檢查左頸腫瘤已消失；而林男也嚇得戒掉長年不離手的菸、酒。

林先生表示，先前有醫學中心醫師曾診斷說「腫瘤已壓到靜脈」，開刀手術不敢說有把握，只能拚拚看。林男因此改找上安南醫院放射腫瘤科主任梁永昌協助，而林男擔心放射治療有嚴重副作用，期間還一度猶豫。

梁永昌向病患詳細說明「階段式隨形影像導引強度調控放射治療」搭配化學治療，可針對腫瘤分布型態與擴展範圍，做出客製化的治療，取得患者認同。這種階段式隨形治療，可因應腫瘤大小與形狀變化適時調整，可極大化或極小化腫瘤放射劑量，減少副作用，讓患者治療後有較好品質社交活動與存活率。



電腦斷層掃描顯示其頸部有腫脹的腫瘤（雷射光點處）。（記者王俊忠翻攝）

口腔吞嚥正常 未感受副作用痛苦

梁永昌說，從8月底開始做放療，患者原本黏固不動的舌頭在治療兩週後能正常活動，左頸腫塊迅速變小，開始恢復口腔進食、體重慢慢增加，體能活動正常。林男直言，很驚訝約7週療程沒感到什麼副作用的痛苦，只要避免辛辣刺激性食物，口腔吞嚥正常。

梁永昌表示，放射治療計畫逐步階段式調整，目的要正常組織器官接受劑量隨之降低，大幅減少口咽部位副作用，生活不受影響。

喜上加喜的是，林男完成療程後1個月回安南醫院做磁振攝影檢查，原來的腫瘤及頸部淋巴都消失不見，讓林男開心感謝醫師是恩同再造。

梁永昌強調，針對頭頸癌患者一律採用個體化、隨形影像導引強度調控放射治療模式進行，可更有效控制腫瘤、減少痛感，讓病人在癌後生活能與正常人一樣，不過，後續仍須定期追蹤、維持良好生活、飲食習慣，防止腫瘤再上身。

自由時報

醫師呼籲，只要有菸、酒、檳榔的過去史，口腔如出現持久不癒的異狀，都要就醫檢查。（照片提供／洪嘉駿）

妙齡西施狂嚼檳榔 20年後驚罹舌癌

文／洪嘉駿

40歲的方小姐（化名）3個月前口腔內出現不明傷口，她想是熬夜火氣大引起，或者是吃東西不小心咬破皮，應該隔幾天就會好，當下並沒有很在意。

但過了大半個月，傷口依然紅腫疼痛，且用手去按壓傷口處，感覺有一個小腫塊，她到附近診所就醫服藥，情況並未明顯改善。最近發現傷口處的腫塊變硬變大，且脖子上也摸到硬塊，愈想愈覺得不對勁，於是接受診所醫師轉診至本院。

方小姐張口接受檢查時，她的傷口處表面上像是一般的潰瘍傷口，但再往傷口底下探觸，才發現這僅是冰山的一角，病灶呈現硬塊觸感，直往舌頭內部發展，在深部有摸到一個硬塊，懷疑病情不單純，直覺是惡性腫瘤，建議進行切片；果然切片檢查後證實是舌癌，而頸部的硬塊則是淋巴轉移，在癌症分期上已屬第三期。

口腔癌、下咽癌、舌癌，都屬於頭頸部腫瘤，在臨床上，罹患頭頸部腫瘤的病人以男性居多，大都長期有抽菸、喝酒、嚼檳榔的習慣，尤其是嚼檳榔，方小姐只有40歲，以頭頸部癌來說相對年輕，又是女性，因此容易輕忽。

經詢問病史，方小姐表示，約20年前做過好幾年檳榔西施，除了把它當口香糖吃，有時是要試包料的口味，有時是客人請吃，當時幾乎每天都吃檳榔，但換工作後，已經很久沒碰檳榔了。

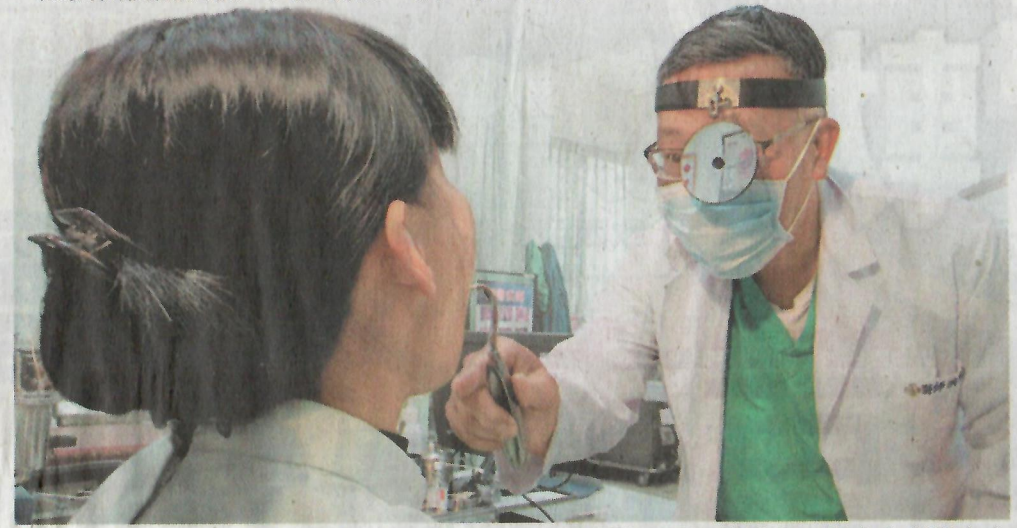
方小姐罹患舌癌不排除和嚼檳榔有關，雖然事隔多年，但當年長時期嚼檳榔的傷害已經造成，建議她儘快接受手術治療。

原本她還擔心手術要切除舌頭及頸部淋巴清除，會影響吞嚥功能、傷害聲帶、損及顏面美觀，但在與醫療團隊充分討論後，她清楚整個治療過程已比傳統手術進步許多，對於外觀及功能的影響也大幅降低，整形外科的重建手術介入也讓結果更為完美。

方小姐術後一個月已能自主呼吸、正常進食，預後很不錯，但還是要接受放射和化學治療，並持續門診追蹤，以防復發的可能。

此實例提醒我們，只要有菸、酒、檳榔過去史的民眾，若口腔出現持久不癒的症狀，都應提高警覺，儘速就醫，才能早期發現，早期治療，這是治療成功與否最重要的關鍵。

（作者為彰化秀傳紀念醫院耳鼻喉科主任）



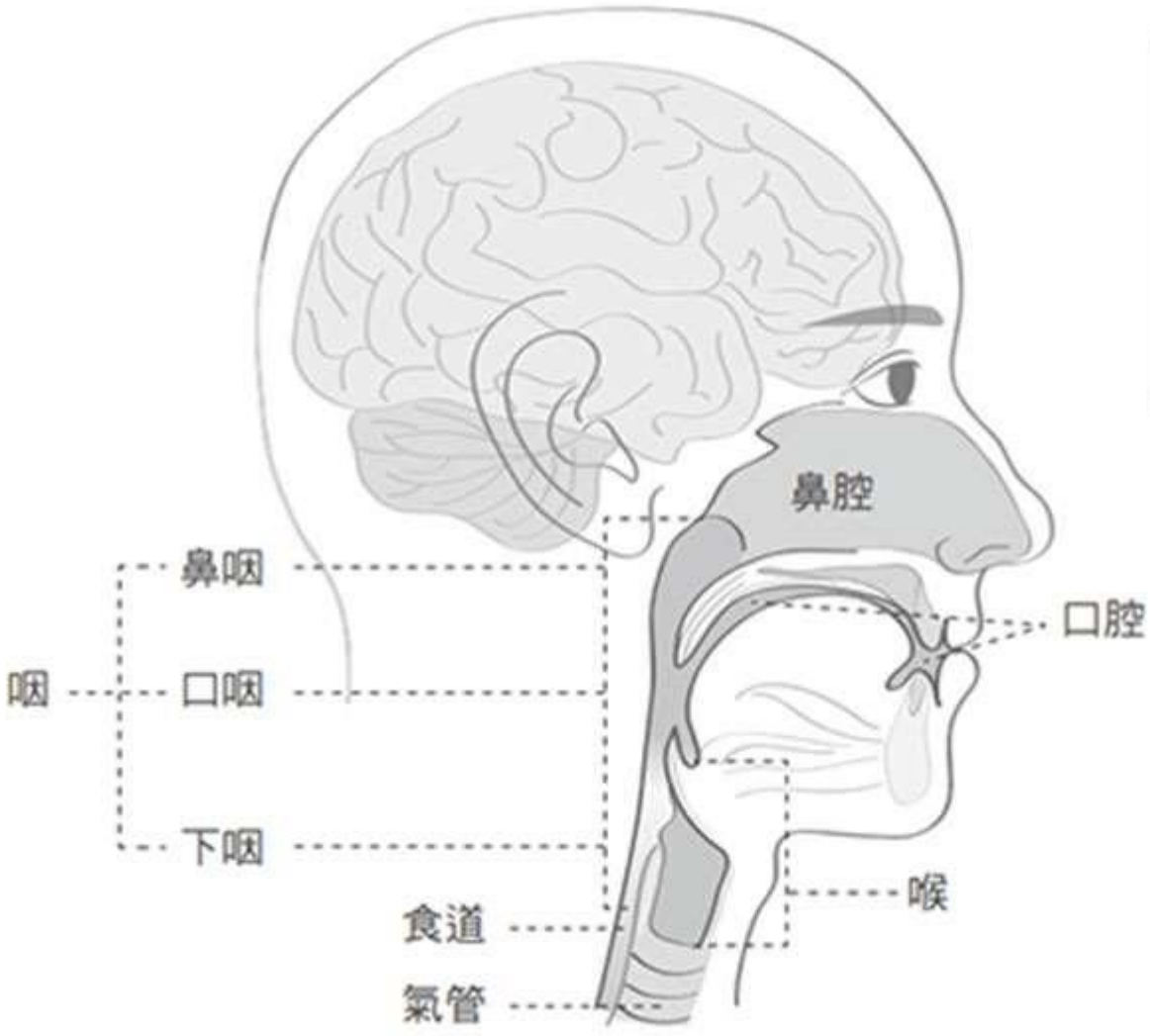
口腔檢查可儘早確診病變，有口腔問題應儘早求醫；圖為情境照，圖中患者與本文無關。（照片提供／洪嘉駿）

特愛找青壯年男性！頭頸癌三大致病原因要小心

想要全面防堵頭頸癌，就要遠離致病原因、危險因子，找回兩大關鍵修護：提升免疫、良好生活習慣，加上留意身體狀況，定期檢查，才有可能樂不思「頭」，高「頸」無憂。

頭頸癌，顧名思義就是位於頭頸部位的腫瘤，近年來一直位列台灣「十大癌症」之一，而且有年輕化與持續上升的趨勢！

資深藝人徐風罹患口腔癌、香港電影最佳綠葉「大傻」成奎安，正值中壯年，卻因為鼻咽癌相繼離世，令許多觀眾相當不捨；韓國年輕偶像金宇彬，更驚傳罹患鼻咽癌，目前積極治療中，使得頭頸癌議題再度浮上檯面。



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頭頸部涵蓋了很多器官，就結構來講，大致上分成口腔、口咽、下咽、喉。

以口咽為中心點，往下是下咽以及喉；而舌頭則是包含在口腔及口咽。從口咽往上，則有鼻腔、鼻竇，鼻咽則是在口咽的正上方。當然，唾液腺也是分屬於此部分。

理論上，甲狀腺剛好位於交界的地方，並沒有歸類在頭頸部的腫瘤，偏向於新陳代謝科、耳鼻喉科、一般外科、核醫科以及腫瘤科進行整合治療，所以，本書不會討論到甲狀腺癌。

頭頸癌大多是局部復發，而且較為容易遠端轉移在肺部、骨頭、肝臟等部位。鼻咽癌則是比較容易遠端轉移的癌症，可能一復發大多都遠端轉移，這也是頭頸癌跟鼻咽癌的不同之處。

三大致病原因，頭頸部染疾上身！

「一名年輕男子因為喘不過氣，緊急送入加護病房，才知道罹患下咽癌第四期！」

「喉嚨老是卡卡、體重莫名減輕的櫃姐，沒想到竟是喉癌！」

「日本女星嘴破只擦藥，就醫發現口腔癌，只好割舌保命！」

以上這些案例乍看相當駭人，然而其實就發生在我們的生活周遭，由於頭頸癌並沒有明顯的症狀，許多人往往容易忽略，因此要是發現自己有嘴破、乾咳、聲音沙啞、耳悶耳脹、呼吸困難、脖子腫脹……類似情況，小心，記得趕緊就醫，進一步全面檢查。

頭頸癌可說是一種高致死的癌症，特別是位列「十大癌症」的口腔癌，一直以來有著「短命癌」的稱號，在於早期不易發現，發現多是中晚期。且術後容易局部復發、擴散，若是伴隨遠端轉移，比較常轉移到肺部、骨頭、肝臟等部位，五年的存活率不高過 20%，成為迅速奪命的劊子手！

以下彙整造成頭頸癌的致病原因，包括：HPV、EBV、暴露危險因子：

- **人類乳突病毒（Human Papillomavirus, HPV）**

人類乳突病毒（HPV），屬於一種 DNA 病毒，其中包括一百多種類型的病毒，其中約有 40 種會感染人類的生殖器官。

有一些頭頸癌是因病毒感染造成，像是人類乳突病毒（HPV）的感染，進而造成頭頸癌病變，其中歐美與亞洲的感染分布不太一樣，可能是因為種族上的差異。

再則，很多人可能會問：「到底是如何會產生這些病毒的？」一般人類乳突病毒存在於子宮頸癌裡面，如果發生性行為，比方說口交，口腔因為接觸，自然就暴露在病毒當中，進而造成感染。

- **人類皰疹病毒第四型（Epstein-Barr virus, EBV）**

EBV 是鼻咽癌的病毒，也是鼻咽癌跟其他頭頸癌不同的地方。

根據統計，有超過 90%的人口受到 EBV 的感染，其中主要是經由唾液傳染而來，患部大致分布於鼻咽、鼻腔、口腔、口咽。

由於鼻咽位於腦袋的正下方，因為結構與位置的差異，因而有別於其他頭頸癌，早期頭頸癌患者通常會採取手術方式進行治療，但是鼻咽因為靠近腦袋瓜下面，一般都是採用放療，或再加上化療。

- **長期暴露於危險因子——抽菸、喝酒、吃檳榔**

任何會傷害口腔、臉頰、食道、黏膜的食物與動作，自然與頭頸癌及食道癌脫離不了關係，口咽癌及喉癌常常伴隨食道癌，舉凡抽菸、喝酒、吃檳榔，長期暴露在危險因子裡面，高風險族群可能就是你！

抽菸不僅僅只是尼古丁的問題，當你點燃一根菸，當中大概就會產生 4 千多種的化學有毒物質，尼古丁只是讓人成癮，但是裡面的已知有 69 種的致癌物質，才是最關鍵的致病原。

抽菸不只增加罹患肺癌的風險，因為霧氣會經過食道、胃、肝臟，更會提高頭頸癌、食道癌和胃癌的機率，甚至是肝癌，所以反而不是尼古丁讓人得到癌症，而是點燃後的有毒化學物質。

「醫師，我沒有抽菸，為什麼也得到口腔癌？」別忘了，二手菸同樣會造成致命影響，當我們吸入有毒物質的物質，那些致癌物一樣會進到身體裡面。

另外，飲用過烈的酒精飲料，也會對口腔造成傷害，就像是在醫院內進行病人或團體衛教時，我常常會加強宣導這些觀念。

「有些人喜歡喝很燙的湯，自然會對黏膜造成破損，雖然也許很快就修復了，但是這樣子反覆傷害黏膜，導致細胞一再受到破壞、修復、破壞、修復的循環刺激，最後有可能會癌化喔！」

「啊，這麼嚴重喔？」一名中年主婦吃驚地摀住嘴巴。

「沒錯，就是因為細胞反覆的發炎，修復過程中有基因出錯，就成為不好的細胞了。」我笑笑地說。

所以，平日飲食要留意減少口腔的刺激，不要喝太燙的湯，才不會造成黏膜反覆破損與修補。

此外，檳榔更是直接造成口腔傷害的刺激物，過度嚼磨一種東西，就容易發生問題，除了成分裡含著有毒物質之外，檳榔的粗纖維極為容易磨損黏膜，所以經常性吃檳榔的話，容易造成口腔纖維化（口腔黏膜下纖維化症），不可不慎。

頭頸癌，特愛找青壯年！

綜合以上各種頭頸癌的常見症狀發現，頭頸癌的早期症狀，並不明顯又無特異性，加上病患本身的疏忽，或是第一線的醫師未能提高警覺，以至於往往失去早期診斷的先機而延誤治療。

此外，應該歸咎在生活中的種種不良習慣，可能是為了「提神」效果而嚼食檳榔，因而產生比例連結。其實癌症的產生，大概一兩成都是跟基因有關係，八成才是後天環境的影響，如果不特別講什麼癌的話，都是這樣的通則。

當然基因有很多未解的謎團，不能說哪種基因就會造成哪種癌症，現在還不夠清楚。不過，現在比較明確的疾病是遺傳性大腸直腸癌，家族性大腸瘜肉症指的就是大腸裡面產生了很多瘜肉，可能是上百顆瘜肉，那個就是遺傳，基因上就有影響，所以才會在一、二十歲，二、三十歲就出現。

至於 80%的後天遺傳，好歹也要暴露個幾年，或暴露一段時間，才會受到後天環境影響，好發在四、五十歲。

頭頸癌的族群的話，好發還是在青、壯年這段期間，大概 30 到 50 歲中間，屬於一個高峰期。臨床上年輕的比較少，然而鼻咽癌的確是有比較年輕一點，因為鼻咽癌主要還是跟免疫力有關係。

男女比例來說，大部分八成都是男性，當然一樣也是暴露在危險因子，抽菸、吃檳榔的比例比較高，另外，社經地位比較低一點的也比較容易罹患，也可以

回過來看，可以說與工作性質、抽菸、喝酒息息相關，因此鼻咽癌就會跟其他頭頸癌比較不一樣。

由於頭頸癌的族群往往相對弱勢，治療的部分，很多化療健保都沒有給付，每次醫療費就是幾萬塊，雖然化療類藥物還是相對比較便宜的，但對於社經地位比較低的族群來說，還是一種負擔。這方面的資源連結，還是要回歸社工那一塊，看看有沒有符合低收入戶資格，或其他社會福利資源。

自我檢視，10 種頭頸癌初步症狀

一、頸部出現不對稱性腫塊。

二、口咽腔內出現超過兩星期的潰瘍、凸起，或是斑點。

三、口腔內長有不明白斑。

四、脖子莫名腫脹。

五、聲音沙啞。

六、單側鼻塞、反覆性流鼻血。

七、單側聽力不良、單耳積水、耳脹、耳悶、耳朵痛。

八、喉嚨老是卡卡。

九、體重莫名減輕。

十、 無上呼吸道感染，卻持續性喉嚨痛，經常感覺喘不過氣。

（首圖／Shutterstock Nattasak Buranasri）

（本文作者為三軍總醫院血液腫瘤科主治醫師；原圖文刊載於陳佳宏《戰勝頭頸癌》／博思智庫）

台灣復健醫學會 癌症復健衛教手冊 | 6

頭頸癌的肩頸復健簡介

【感謝】本文宣內容製作經費由國民健康署菸品健康福利捐支應

一、頭頸癌患者肩頸部常見問題

- 頭頸癌患者常見肩頸痠痛、僵硬、活動受限等不適。除了腫瘤本身的影響，再加上手術及後續的放射線治療等，皆可能造成肌肉軟組織纖維化、關節攣縮、淋巴回流受阻、神經壓迫及傷害等併發症，進一步惡化肩頸症狀，造成緊繃感、活動受限、肩膀疼痛、上肢無力等問題，嚴重影響病患的功能及生活品質。
- 接受放射治療後數月至數十年間，仍有可能發生遲發性的軟組織纖維化，尤其以治療後2~5年為好發的高峰期。軟組織纖維化將造成肩頸部的活動受限，進一步造成肩頸區域的肌肉緊繃及疼痛。

二、患者正確的姿勢擺位及居家自我照護建議

- 頭部後拉、收下巴、擴胸，維持端正挺拔姿勢：可鍛鍊後肩頸肌肉，避免胸肌緊縮。

錯誤姿勢
（駝背、屈頸、圓肩）

正確姿勢
（頭部後拉、收下巴、擴胸）

- 倘若合併肩部下垂無力：
  - ◇ 坐姿：宜將無力手置於桌子或是扶手上。
  - ◇ 站姿：可將無力手置於口袋中，提供支撐並減少肩膀受力，預防肩頸肌肉拉傷。

- 睡覺時宜仰躺。若需側躺，宜讓健側在下，避免將患側壓在下方。並於身體前方放置枕頭支撐患側上肢，減少肩頸肌肉的拉扯。
- 剛接受手術後，應避免用患側上肢提重物（勿大於1.5kg，約2瓶700c.c.大杯裝飲料）。
- 手術及放射治療後避免使用肩背包。並請教您的醫療團隊評估何時能恢復使用。

三、患者自主症狀篩檢／尋求復健科或手術醫師協助的時機

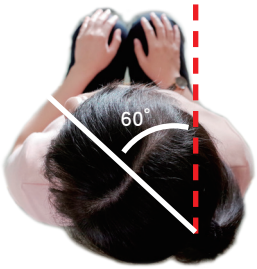
- 術後4~6週，肩頸關節活動度應達到以下標準。若無法達到下述標準或持續惡化，宜洽詢您的復健科醫師。

  ◇ 頭向肩膀側傾斜可達45度。

  ◇ 頭側向旋轉可達60度。

  ◇ 肩膀前抬可貼近耳朵。

頭側傾應達45度



頭側轉應達60度

肩膀前抬可貼近耳朵

何時應尋求醫師協助？

- 肩頸部位僵硬、腫脹、疼痛。
- 肩頸肌肉明顯萎縮。
- 越來越嚴重的上肢麻、脹、刺痛、感覺異常。
- 手術傷口癒合不佳、流血或顏色發黑。

- 肩頸紅、腫、熱、痛、流膿，或合併發燒。
- 呼吸困難，傷口新出現硬塊。

四、復健科醫師可能會給您的診斷及治療計畫

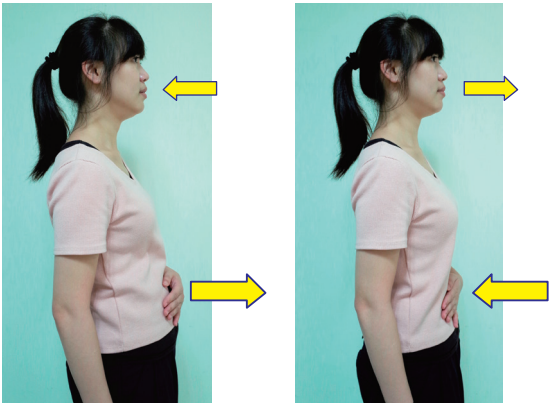
完善的復健評估，包含診斷及釐清根本原因，提供個別化的復健計畫，以達到止痛、增進肩頸關節活動度、強化肌耐力等目標，維持良好的生活品質與功能。

- 執行理學檢查，安排抽血、X光、超音波、神經功能等檢查。
- 口服藥物治療。
- 局部注射治療。
- 儀器治療。
- 治療性運動（包含關節鬆動術、牽拉運動、淋巴引流治療、肌力訓練）。
- 個人化居家運動計畫、評估及諮詢。
- 安排轉診至相關科別。

五、患者居家自我照顧及運動治療

- 運動目標：維持肩頸關節活動度，避免肌肉緊繃、萎縮。
- 自主運動開始時機：待引流管拔除及傷口癒合後，即應開始積極自主運動。
- 運動強度：針對每項建議運動，每天至少早晚各做一回合。未接受放射治療患者應維持至少三個月。若有接受放射治療者，運動維持期需要更長，以避免遲發性的放療副作用（如：軟組織纖維化）。
- 運動注意事項：
  - ◇ 運動時維持正常呼吸，避免憋氣。
  - ◇ 動作宜慢、輕、柔、穩定。避免因過快的拉扯而造成傷害。
  - ◇ 剛開始學習時，可照鏡子來評估自己的動作是否正確。
  - ◇ 以不讓組織再度受傷為原則。傷口癒合不良、皮膚黏膜破裂、肌肉肌腱發炎時，應暫時休息。
  - ◇ 如果運動過程中有疼痛不適，請暫停運動並洽詢您的醫療復健團隊。

- 腹式呼吸（Diaphragmatic breathing）
  - ◇ 起始動作：坐在有靠背的椅子上。
  - ◇ 雙手輕輕置於肚子上方（丹田）。
  - ◇ 吸氣：緩慢吸氣，感受肚子逐漸膨脹（氣湧丹田），並使胸口盡量維持不動。
  - ◇ 吐氣：緩慢吐氣，感受肚子逐漸收縮變平坦，並使胸口盡量維持不動。
  - ◇ 重複10次以上。
  - ◇ 掌握要領後，隨時隨地都可做。

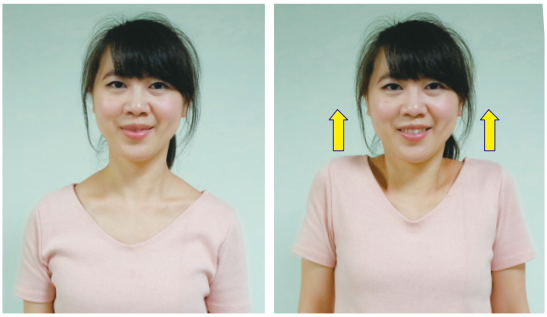


吸氣動作：肚子膨脹（氣湧丹田）　　**吐氣動作：肚子壓縮**

- 胸鎖乳突肌肌力訓練（Sternocleidomastoid muscle strengthening）
  - ◇ 採平躺仰臥姿勢，雙手抱胸。
  - ◇ 在肩膀不離開床的前提下，把頭抬起前屈，盡可能看向自己的腳趾，出力維持10秒後，放鬆回到起始動作。
  - ◇ 上述動作期間務必注意正常韻律呼吸，切勿憋氣。
  - ◇ 持續5次。

**註：接受氣切手術的患者，欲執行此動作前，請先諮詢您的復健科醫師。*

- 聳肩運動（Shoulder shrugs）
  ◇ 將兩側肩膀往耳垂方向聳肩，出力維持約10秒。
  ◇ 重複5次。



- 斜方肌肌力訓練（Trapezius muscle strengthening）
  ◇ 起始動作：患側上肢自然下垂伸直。
  ◇ 手持約半公斤重的啞鈴（或約600ml的寶特瓶裝水）。
  ◇ 將手臂緩慢外展平舉，至120度左右，出力維持10秒鐘。
  ◇ 重複5次。
  **註：重量可逐漸增加，以不會造成肩部不適的最大重量為原則。*

- 肩胛回縮運動（Arm and shoulder retraction）
  - ◇ 雙上臂外展，雙肘彎曲90度，使五指朝天手心朝前。
  - ◇ 盡可能地使肩胛骨做回縮的動作，持續出力10秒鐘後放鬆，回到起始動作。
  - ◇ 重複5次。

- 轉頸伸展（Turning neck stretch）
  - ◇ 輕柔地轉頭，使眼睛往右上方看。
  - ◇ 將您的右手置於左側的臉頰及下頷上，順著眼睛的方向輕輕施力，令左側前頸得以伸展，維持1分鐘。
  - ◇ 輕柔地轉頭，使眼睛往左下方看（與上一動成對角線姿勢）。
  - ◇ 將您的左手置於頭的右上方，提供一個向下伸展右側後頸的力量，維持1分鐘。
  - ◇ 上述動作重複5次後，轉換另一組對角線方向（左上右下），再做5次。

- 側頸伸展（Side neck stretch）
  - ◇ 盡可能地將右臂向外下方伸展。
  - ◇ 將您的左臂置於頭上，並輕輕的將頭往左側拉動，以伸展右頸肌群。
  - ◇ 持續1分鐘後，放鬆回到起始動作。
  - ◇ 重複5次後，換邊。

- 後頸伸展（Posterior neck stretch）
  - ◇ 雙手抱頭。
  - ◇ 以雙手將頭往前下方牽拉，使後頸得以伸展，維持1分鐘後，放鬆回到起始動作。
  - ◇ 重複5次。

- 擴胸伸展運動（Pectoral stretch）
  ◇ 站立在90度轉彎牆角。
  ◇ 雙肘向上彎曲約90度，上臂外展與肩齊平，前臂置於牆壁上。
  ◇ 單腳輕輕地往前踏一步，並感受到胸肌因伸展而緊繃的感覺。此時盡量打直腰桿，並使肩頸肌肉維持放鬆。
  ◇ 持續1分鐘，回到起始動作。
  ◇ 重複5次。
  **註：上臂的位置可分為高過肩膀（約外展120度）、與肩齊平、低於肩膀（約外展60度）等三個角度分別執行。*

結語

頭頸癌的治療成效逐年進步，歷經辛苦的腫瘤治療後，存活期已逐漸增長。在抗癌徬徨、煎熬的日子裡，若能有家人持續地支持與陪伴，再加上復健團隊介入和功能重建，協助抗癌鬥士們可以克服身體的障礙，迎向自主獨立、有品質的生活，是指日可待的！

癌症復健衛教系列

頭頸癌的肩頸復健簡介

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Review

Evolution in the management of oropharyngeal squamous cell carcinoma: systematic review of outcomes over the last 25 years

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Abstract

The treatment of oropharyngeal squamous cell carcinoma (SCC) has evolved over the last 25 years, from open surgery to combined chemoradiotherapy, and now to the development of minimally invasive procedures, but evidence for the best treatment is lacking. We therefore did a systematic search of the MEDLINE database for studies published between 1992 and 2017 that reported oncological or functional outcomes, or both. Predefined inclusion and exclusion criteria were used for screening and selection, and 45 studies were chosen. Only one was a randomised controlled trial, all the rest were prospective or retrospective case series. The heterogeneities in their characteristics made meta-analysis impossible and only qualitative analysis was feasible. We found no conclusive evidence to suggest the advantage of one therapeutic approach over another, so we still cannot offer patients the "ideal" treatment. We have, however, raised the possibility of there being two different entities: human papillomavirus (HPV)-positive and HPV-negative disease.

Keywords: Oropharyngeal Squamous Cell Carcinoma; Management; Treatment; Outcomes; Systematic Review

Introduction

The incidence of oropharyngeal squamous cell carcinoma (SCC) is rising throughout the developed world, particularly in North America, Northern Europe, and Taiwan.[1,2]

In 2007, the International Agency for Research on Cancer (IARC) reported that the human papillomavirus (HPV) type16 was a cause of both oropharyngeal and oral cavity cancer[3] (until then, the main causes had been thought to be consumption of tobacco and alcohol). Recent studies have shown that HPV causes more than 5% of cancers worldwide, including all cervical, and an increasing proportion of oropharyngeal cancers.[4] The incidence of oropharyngeal SCC has been predicted to surpass that of cervical cancer in some developed countries,[5] and currently, the number of patients with the disease worldwide affects the resources that are available because so many cases are now attributed to the virus.

The oropharynx should be considered as a separate entity from the rest of the head and neck because of its distinctive anatomical and histological features. A recent American epidemiological study that included four decades of data (1973–2012) confirmed that cancers of the oral cavity and pharynx do not have a single cause. It showed that the incidence of most cancers of the oral cavity (vestibular cancers,

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and those of the lip, gum, floor of the mouth, hard palate, and buccal mucosa) had declined considerably as a result of a reduction in smoking in the United States, but that the incidence of oropharyngeal cancers and cancers of the tongue had increased to a similar extent in both sexes. Age-period-cohort analyses have shown increases in the incidence of oropharyngeal cancers and those of the tongue, but the greatest increase was in oropharyngeal cancers.[6]

The prevalence of HPV in oropharyngeal SCC has also increased considerably in the European population. A 2016 multicentre cross-sectional retrospective study on patients diagnosed between 2002 and 2011 in the United Kingdom showed that although the number of cases had nearly doubled, the proportion of those without HPV remained at roughly 50%.[7] Results were similar in East Germany (1998–2011). Compared with the United States, the epidemiological shift over recent decades in European countries from HPV-negative to HPV-positive disease seems to have been delayed because of minor behavioural changes (consumption of alcohol and tobacco smoking).[8] According to the conclusions of these studies, however, the rapid increase in the incidence of oropharyngeal SCC cannot be attributed solely to the influence of HPV.

The oropharynx comprises the base of the tongue, soft palate, palatine tonsillar fossa, and pharyngeal wall. The palatine and lingual tonsils, together with the pharyngeal (adenoid) and tubal tonsils of the nasopharynx, form a circular area of mucosa-associated lymphoid tissue (MALT) known as Waldeyer's tonsillar ring.

Histologically, the mucosa of this region is distinct from other mucosal surfaces, as it is composed of lymphoepithelium, a reticulated epithelium with a discontinuous basement membrane. The palatine tonsils have the most convoluted and deep crypts, followed by the lingual tonsils. The adenoids and tubal tonsils contain less of this lymphoid tissue.

SCC accounts for more than 95% of tumours of the oropharynx. The lack of a consistent basement membrane in the palatine and lingual tonsils precludes the possibility of the disease being restricted by their surfaces (SCC in situ tends to occur only in the soft palate and pharyngeal wall), and more than 60% of patients with SCC of the oropharynx (notably of the tonsil and base of the tongue) present with involved cervical lymph nodes. Between 10% and 15% have distant metastases.[9]

Anatomically, the oropharynx is the intersection between the airway and digestive tract, and it has a strategic role in the swallowing process. Surgery and radiological interventions for oropharyngeal SCC can damage the pharyngeal tissues and result in obstruction, xerostomia, stenosis, or lack of muscular coordination, and will eventually lead to dysphagia.

The ultimate goal of treatment is to cure, prevent secondary tumours or recurrence, preserve function (speech, swallowing, and taste), and minimise complications. To achieve this, management has evolved, and the Veterans Affairs Laryngeal Cancer Study in 1991, which showed the effectiveness of chemoradiotherapy to preserve the larynx in cases of advanced cancers (stage III or IV),[11] established the conversion from surgical management to organ preservation. This new approach resulted in the adoption of combined chemoradiotherapy alone as the first-line treatment for oropharyngeal SCC despite a lack of studies and evidence.

Currently, when operation is the first method of treatment, minimal access techniques such as transoral laser microsurgery or transoral robotic surgery (TORS) are used. Two-dimensional radiotherapy has evolved into less toxic intensity-modulated radiotherapy (IMRT), and new de-escalations in protocols for chemoradiation have been studied to reduce complications.[12]

Decisions about the best approach should take these changes into account.

We know of no recommended published guideline that compares the effectiveness of different treatments in terms of oncological and functional outcomes. The purpose of this systematic review therefore was to establish whether these changes in the treatment and management of oropharyngeal SCC over the last 25 years have improved outcomes in terms of disease control, maintenance of function, and reduction in toxicity.

Aim

All patients studied were treated with curative intent. We compared the results of the different treatments (conventional and minimally-invasive surgery, radiotherapy, chemotherapy, or a combination) and used the oncological and functional outcomes as benchmarks for success. Our main objective was to find out which, if any, is the most effective.

Material and methods

Electronic search strategy

For this systematic study, we developed a detailed search strategy in collaboration with a specialist librarian. We searched the MEDLINE database in May 2017 for all original studies published between 1992 and 2017 using the following search terms: "oropharyngeal", "squamous cell carcinoma", "management", "treatment", "surgery", "minimally invasive surgery", "minimally invasive procedures", "outcomes", "salvage", "response to treatment", "neoadjuvant chemotherapy", "induction chemotherapy", "chemoradiation", "radiotherapy", "radiation therapy", "intensity-modulated radiation therapy", "target therapy", and "targeted drugs".

We considered only studies in the English language and those on human subjects.

All the papers included focused on the oncological or functional outcomes, or both, of treatments for oropharyngeal SCC. They reported original research including randomised trials, cohort studies, case control studies, retrospective and prospective observational studies, and case series of more

than 10 patients. Overviews, reviews, meta-analyses, and papers that did not focus on the treatment and outcomes of patients with oropharyngeal SCC, together with those that included fewer than 10 patients, or patients with tumours in other sites (nasopharynx, hypopharynx, larynx, or oral cavity), were excluded.

Search for other resources

We also searched the references of the papers included and other reviews of the treatment of oropharyngeal SCC (not included in the study) to identify further relevant papers.

Review process

Two reviewers assessed the titles and abstracts for relevance. If the abstract did not clearly state the site of the tumour, the full text was screened. Full texts of all the papers included were retrieved, and two authors reviewed them independently for relevance. Any disagreements were resolved by discussion with the third author. The review was conducted according to the Prisma extension statement for the reporting of systematic reviews.[13] No ethics approval was required.

Data extraction and management

The data were extracted independently by both reviewers and stored on a Microsoft Excel spread sheet. In each case we recorded the year of publication, period and design of the study, site and type of treatment, stage of disease, number of patients, follow up, oncological outcome (overall and disease-free survival, and locoregional control), functional outcome (including method of assessment), and complications.

Details of the studies are shown in Table 1.[14–59]

Quality assessment

Table 2 summarises the methodological quality of evidence of each study based on the levels published by the Oxford Centre for Evidence–based Medicine.[60]

Results

Fig. 1 shows the search strategy. A total of 46 papers (45 studies) were finally included. Two papers reported the outcomes of one study (Holsinger et al[44] reported functional outcomes, and Laccourreye et al[45] oncological outcomes).

Study characteristics

Only one of the studies was randomised.[34] Twelve were prospective case series.[34,37,40,46–50,53,54,56,57] All the rest were retrospective case series,[14–33,35,36,38,39,41–45,51,52,55,58,59] of which three were matched for stage of disease.[43,52,55] A total of 27 papers considered all four subsites of the oropharynx,[21–24,27,31,32,34,36–43,47–50,52,53,55–59] ten focused on the tonsil,[15–18,26,33,35,44,45,54] eight on the base of the tongue,[14,19,20,25,29,30,46,51] and one on the lateral wall.[28]

Twenty-one compared different treatments[15–17,20,21,23,25,31,34–38,42,43,52,54–57,59] while 25 did not.[14,18,19,22,24,26–30,32,33,39–41,44–51,53,58]

A total of 27 papers considered all stages of disease.[14–19,23,25,27,28,31–33,36,37,39,44–47,50–53,55,57,59] The rest considered only early[21,22,24,30,40,48,54,56,58] or advanced cancer.[20,26,29,34,35,38,41–43,49] All studies reported different follow-up rates.

A total of 30 papers reported overall survival,[14,15,18,19,22,24–26,28–32,34–36,38,39,41–46,49,51,52,54,57,58] and of them, 19 reported it at five years. A total of 20 reported locoregional control (13 at five years),[15,16,24,25,30–36,38,39,44–46,49,51,57,58] and 23 disease-free survival (15 at five years).[16,17,19,26,28–36,38,39,42,46,49,51,54,55,57,58]

A total of 24 objectively assessed functional outcomes and quality of life.[20–23,27,28,37,40,42–54,56,58,59] Table 3 shows the questionnaires that were used, and Table 4 the objective assessments. In one publication a multivariate analysis had been done to assess the ability to swallow solids, pastes, and liquids.[27]

Complications were reported in 32 publications.[14,15,17–19,21,22,27–29,32–36,38–47,49,51–54,57,58]

We had planned to use the data for statistical analysis, but the heterogeneities in the studies' characteristics (different comparisons and outcome measures) made it impossible.

The data, however, provide an overview of the changes in management during the last 25 years, and to show this, we have grouped the publications chronologically according to approach: conventional surgery, organ preservation, and minimally-invasive surgery.

Conventional surgery

The first retrospective studies from 1993 and 1994 supported aggressive surgery for oropharyngeal cancers, and reported good survival and local control in patients with SCC of the base of the tongue[14] and tonsil.[15] Resection was done through a transoral approach, mandibular osteotomy, partial mandibulectomy, or pharyngotomy. In both studies, adjuvant treatment was suggested only in advanced stages (III and IV) to improve locoregional control. The most common complications were wound infections, partial flap necrosis, and pulmonary compromise. Outcomes for speech and swallowing were satisfactory, but no objective measures were used.[14,15]

In 1998, a retrospective study on tonsillar SCC showed that radiation was a valid alternative to operation for local disease (stage I/II). In cases of advanced disease (stage III/IV), however, five-year local control with radiotherapy alone was

Table 1
Study characteristics.

First author, year, and reference	Group	Site	Management	Stage	No. of patients	Follow up (months)	Oncological outcome			Functional outcome/QoL objective measurement	Reported complications
							Overall survival	Locoregional control	Disease-free survival		
Kraus 1993[14]	1979–1989	BoT	Operation +/− RT	T1,T2,T3,T4	100	Median 39.6	5-year I/II 77%, III 64%, IV 59%	NR	NR	NR	Yes
Foote 1994[15]	1970–1988	Tonsil	Operation cf operation + RT	T1,T2,T3,T4	72 (56 cf 16)	Minimum 42	5-year III 56% cf 100%, IV 43% cf 78%	5-year I 77% cf 78%, II 70% cf 83%, III/IV75% cf 44%	NR	NR	Yes
Hicks 1998[16]	1971–1991	Tonsil	Operation alone cf RT alone	T1,T2,T3,T4	76 (56 cf 20)	Median 42	NR	5-year 75% cf 60%	5-year 61% cf 37%	NR	No
Perez 1998[17]	1959–1991	Tonsil	RT cf preRT + operation cf operation + post RT	T1,T2,T3,T4	384 (154 cf 144 cf 86)	Median 111.6	NR	NR	5-year I 50% cf 50%, II 23% cf 60% cf 50%, III 50% cf 57% cf 62%, IV 58% cf 50% cf 50%	NR	Yes
Galati 2000[18]	1981–1995	Tonsil	Operation +/− RT	T1,T2,T3,T4	162	Minimum 24	5-year I 89%, II 91%, III 79%, IV 52%	NR	NR	NR	Yes
Gourin 2001[19]	1980–1997	BoT	Operation +/− RT	T1,T2,T3,T4	87	Median 38	5-year 49%	NR	5-year I 100%, II 86%, III 62%, IV 48%	NR	Yes
Perlmutter 2002[20]	1976–2000	BoT	Operation cf no operation	T3,T4	61 (43 cf 18)	Median 38.5	NR	NR	NR	3 questionnaires: PSSHN, UW-QoL, history of treatment	No
Pourel 2002[21]	1992–1998	OP	Surgery + RT cf BT +/− EBRT cf EBRT alone	T1,T2,T3	113 (27 cf 49 cf 37)	Median 62	NR	NR	NR	2 questionnaires: EORTC QLQ C30, EORTC H&N35	Yes
Watkinson 2002[22]	1993–2000	OP	Operation + RT	T1,T2	18	Median 45,6	2-year 100%, 5-year 92%	NR	NR	2 questionnaires: EORTC QLQ C30, GHQ-12	Yes
Allal 2003[23]	1981–1998	OP	Operation + RT cf RT +/− CT	T1,T2,T3,T4	60 (20 cf 40)	Median 78 cf 27	NR	NR	NR	2 questionnaires: PSSHN, EORTC QLQ C30	No
Cosmidis 2004[24]	1995–2000	OP	Operation alone	T1,T2 N0	53	Up to 60	1-year 100%, 3-year 94.6%, 5-year 73%	1-year 96.22%, 3-year 92.45%, 5-year 88.68%	NR	NR	No

Barrett 2004[25]	1992–1998	BoT	Operation + RT cf RT cf RT + interstitial RT	T1,T2,T3,T4	53 (17 cf 16 cf 20)	Median 31	5-year 44% cf 24% cf 33%	5-year 74% cf 25% cf 87%	NR	NR	No
Bachar 2010[26]	1970–1990	Tonsil	Salvage operation after RT	NR	175	Up to 60	5-year 23%	NR	5-year 40%	NR	No
Buiret 2011[27]	1998–2003	OP	Operation +/− RT+/− chemotherapy	T1,T2,T3,T4	254	Up to 120	NR	NR	NR	Alimentation multivariate model analysis, NGT dependence, weight loss	Yes
Diaz-Molina 2011[28]	1990–2008	Lateral wall	Operation +/− RT	T1,T2,T3,T4	155	Median 39	5-year 33%	NR	5-year 43%	Tracheotomy duration; NGT dependence	Yes
Rodrigo 2011 [29]	1990–2007	BoT	Transhyoid operation +/− RT	II,III,IV	84	Median 19	5-year 19%	NR	5-year 31%	NR	Yes
Iyer 2013[30]	1985–2005	BoT	Operation +/− CRT	T1,T2	128	Median 68	5-year 60%	5-year 70%	5-year 61%	NR	No
Iyer 2015[31]	1985–2005	OP	Operation +/− RT P16 + OPC cf P16 - OPC	T1,T2,T3,T4	201 (106 cf 95)	Up to 60	5-year 60% (74% cf 44%)	5-year 89%	5-year 76% (84% cf 66%)	NR	No
Fein 1996[32]	1964–1991	OP	RT +/− neck dissection +/− salvage surgery	T1,T2,T3,T4	490	Minimum 24	5-year 44%	5-year 85%	5-year 77%	NR	Yes
Mendenhall 2000[33]	1964–1997	Tonsil	RT +/− neck dissection	T1,T2,T3,T4	400	Minimum 24	NR	5-year T1 83%,T2 81%,T3 74%,T4 60%	5-year I 100%, II 86%, III 82%, IVa 63%, IVb 22%	NR	Yes
Denis 2004[34]	1994–2001	OP	RT cf CRT	III,IV	226 (113 cf 109)	Median 66	5-year 15.8% cf 22.4%	5 year 24.7% cf 47.6%	5-year 14.6% cf 26.6%	NR	Yes
Shirazi 2006[35]	1994–2002	Tonsil	CRT cf operation	T3,T4	74 (38 cf 36)	Median 34.8	4-year 41% cf 71%	4-year 48% cf 71%	4-year 86% cf 94%	NR	Yes

Table 1 (*Continued*)

First author, year, and reference	Group	Site	Management	Stage	No. of patients	Follow up (months)	Oncological outcome			Functional outcome/QoL objective measurement	Reported complications
							Overall survival	Locoregional control	Disease-free survival		
Hodge 2007[36]	1995–2005	OP	IMRT cf RT cf RTpreIMRTera	T1,T2,T3,T4	195 (52 cf 38 cf 105)	Median 30.4	3-year 88.2% cf 81.1% cf 67.7%	3-year 96.1% cf 78.1% cf 88.1%	3-year 97.7% cf 83.5% cf 79.9%	NR	Yes
Yao 2007[37]	1997–2005	OP	IMRT cf conventional RT	T1,T2,T3,T4	53 (26 cf 27)	12	NR	NR	NR	Questionnaire: HNCI HRQoL	No
Rusthoven 2008[38]	1998–2007	OP	3D-CRT cf AFRT-CB cf IMRT	III, IV	87 (23 cf 32 cf 32)	Median 24	2-year 77.3%	2-year 86,4%	2-year 69.5%	NR	Yes
Mendenhall 2010[39]	2001–2007	OP	IMRT	T1,T2,T3,T4	130	Median 42	5-year 76%	5-year 87%	5-year 93%	NR	Yes
Cartmill 2012[40]	2006–2009	OP	AFRT-CB	T1,T2,T3	12	24	NR	NR	NR	Questionnaire: MDADI	Yes
Self 2013[41]	2005–2010	OP	CT without operation	T2,T3,T4	139	24	13.0 months haemorrhages cf 50.0 months haemorrhage	NR	NR	NR	Yes
Lohia 2014[42]	2000–2009	OP	IMRT cf 3D-CRT	T2,T3,T4	159 (103 cf 56)	Median 34.8 cf 57.5	2-year 62% cf 71%	NR	2-year 59% cf 66%	ECOG performance status; NGT dependence;Weight loss	Yes
Dobrosotskaya 2014[43]	2000–2002	OP	CRT carboplatin and cisplatin + RT cf weekly carboplatin + RT	T3,T4	70 (35 cf 35)	36	3-year 71% cf 88%	NR	NR	NGT dependence 26% cf 6%	Yes
Holsinger 2005[*,44] Laccourreye 2005[*,45]	1978–1998	Tonsil	TLO +/− induction CT or RT +/− post RT	T1,T2,T3,T4	191	Mean 120	1-year 87.5%, 3-year 66.2%, 5-year 56.2%	1-year 91.2% 3-year 82.1%, 5-year 82.1%	NR	NGT dependence; tracheotomy duration; hospital stay duration	Yes
Grant 2006[46]	1997–2005	BoT	TLM +/− RT	T1,T2,T3,T4	59	Mean 31	2-year T192%,T2 91%,T3100%,T4 75%, 5-year T1 58%, T2 91%,T3 75%, T4 38%	2-year and 5-year T1 100%,T2 87%,T3 100%,T4 69%	2-year and 5-year: 84%	FOSS, CS	Yes
Moore 2009[47]	2007–2008	OP	TORS +/− CRT	T1,T2,T3,T4	45	1	NR	NR	NR	FOSS, CS	Yes
Sinclair 2011[48]	2007–2010	OP	TORS +/− CRT	T1,T2	42	Median 17	NR	NR	NR	Questionnaire: MDADI	No
Haughey 2011[49]	1996–2006	OP	TLM + neck dissection +/− CRT	III,IV	204	Mean 49	2-year 89%, 3-year 86,5%, 5-year 78%	NR	2-year 85%, 3-year 82%, 5-year 74%	NGT dependence; FOSS, hospital stay duration	Yes

Leonhardt 2012[50]	2007–2008	OP	TORS +/− CRT	T1,T2,T3,T4	38	12	NR	NR	NR	2 questionnaires: PSSHN, SF-8 health survey	No
Canis 2013[51]	1986–2007	BoT	TLM +/− CRT	I,II,III,IV	82	Median 51	5-year I–II 70%, III 44%, IV 58%	5-year I–II 94%, III 78%, IV 81%	5-year I–II 86%, III 54%, IV 69%	NGT dependence	Yes
White 2013[52]	2003–2011	OP	Salvage surgery: TORS cf open surgery	T1,T2,T3,T4	128 (64 cf 64)	24	2-year 74% cf 43%	NR	NR	NGT dependence; tracheotomy duration; hospital stay duration	Yes
Dziegielewski 2013[53]	2008–2012	OP	TORS	T1,T2,T3,T4	81	Mean 22.7	NR	NR	NR	Questionnaire: HNCI HRQoL; NGT dependence; hospital stay duration	Yes
Lee 2014 [54]	2008–2011	Tonsil	TORS cf conventional surgery	T1,T2,T3	57(27 cf 30)	Mean 20.3	2-year 100% cf 96.7%	NR	2-year 95,6% cf 91,6%	2 questionnaires: VHI 10, MDADI; NGT dependence	Yes
Ford 2014[55]	2004–2012	OP	TORS cf open surgery	T1,T2,T3,T4	130 (65 cf 65)	36	NR	NR	1-year 94% cf 85%, 2-year 91% cf 75%, 3-year 89% cf 73%	NR	No
O'Hara 2015[56]	2011–2013	OP	TLM +/− CRT cf CRT	T1,T2,T3	56 (23 cf 33)	3	NR	NR	NR	Questionnaire: MDADI; Normalcy of Diet Scale (subsection of PSSHN); WST time	No
Smith 2015[57]	2000–2009	OP	TORS + neck dissection cf CRT	T1,T2,T3,T4	70 (42 cf 38)	33	3-year 83% cf 57%	3-year 90% cf 74%	3-year 94% cf 85%	NR	Yes
Chauhan 2015[58]	2010–2014	OP	TLM	T1,T2	12	Median 15	1-year 82%	1-year 100%	1-year 100%	NGT dependence	Yes
Zevallos 2016[59]	2010–2011	OP	TORS cf non-robotic transoral surgery	T1,T2,T3,T4	514 (369 cf 145)	1	NR	NR	NR	30 days readmission	No

cf = compared with; QoL = quality of life; BoT = base of tongue; RT = radiotherapy; NR = not reported; PSSHN = performance status scale for head and neck cancer patients; UW-QoL, University of Washington quality of life instrument; OP = oropharynx; BT = brachytherapy; EBRT = external beam radiotherapy; EORTC = European Organisation for Research and Treatment of Cancer; GHQ = General Health Questionnaire; CT = chemotherapy; NGT = nasogastric tube; CRT = chemoradiotherapy; OPC = oropharyngeal cancer; IMRT = intensity-modulated radiotherapy; HNCI HRQoL = Head and Neck Cancer Inventory health-related quality of life; 3D-CRT = 3-dimensional conformal radiotherapy; AFRT-CB = accelerated fractionation radiotherapy with concomitant boost; MDADI = MD Anderson Dysphagia Inventory; ECOG = Eastern Cooperative Oncology Group; TLO = transoral lateral oropharyngectomy; TLM = transoral laser microsurgery; FOSS = Functional Outcome Swallowing Scale; CS = Communication Scale; TORS = transoral robotic surgery; S = short form; VHI = Voice Handicap Index; WST = water swallow test.

* Holsinger et al[44] and Laccourreye et al[45] reported outcomes from the same study.

Table 2
Methodological quality of evidence based on the Oxford Centre for Evidence–based Medicine.

First author and reference	Year	Study design	Level of evidence
Kraus[14]	1993	Retrospective	4
Foote[15]	1994	Retrospective	4
Hicks[16]	1998	Retrospective	4
Perez[17]	1998	Retrospective	4
Galati[18]	2000	Retrospective	4
Gourin[19]	2001	Retrospective	4
Perlmutter[20]	2002	Retrospective	4
Pourel[21]	2002	Retrospective	4
Watkinson[22]	2002	Retrospective	4
Allal[23]	2003	Retrospective	4
Cosmidis[24]	2004	Retrospective	4
Barrett[25]	2004	Retrospective	4
Bachar[26]	2010	Retrospective	4
Buiret[27]	2011	Retrospective	4
Diaz-Molina[28]	2011	Retrospective	4
Rodrigo[29]	2011	Retrospective	4
lyer[30]	2013	Retrospective	4
Iyer[31]	2015	Retrospective	4
Fein[32]	1995	Retrospective	4
Mendenhall[33]	2000	Retrospective	4
Denis[34]	2004	Prospective randomised	3B
Shirazi[35]	2005	Retrospective	4
Hodge[36]	2007	Retrospective	4
Yao[37]	2007	Prospective non-randomised	4
Rusthoven[38]	2008	Retrospective	4
Mendenhall[39]	2010	Retrospective	4
Cartmill[40]	2011	Prospective non-randomised	4
Self[41]	2013	Retrospective	4
Lohia[42]	2014	Retrospective	4
Dobrosotskaya[43]	2014	Retrospective matched	4
Holsinger*,[44]	2005	Retrospective	4
Laccourreye*,[45]			
Grant [46]	2006	Prospective non-randomised	4
Moore [47]	2009	Prospective non-randomised	4
Sinclair[48]	2011	Prospective non-randomised	4
Haughey[49]	2011	Prospective non-randomised	4
Leonhard[50]	2012	Prospective non-randomised	4
Canis[51]	2013	Retrospective	4
White[52]	2013	Retrospective matched	4
Dziegielewski[53]	2013	Prospective non-randomised	4
Lee[54]	2014	Prospective non-randomised	4
Ford[55]	2014	Retrospective matched	4
O'Hara[56]	2015	Prospective non-randomised	4
Smith[57]	2015	Prospective non-randomised	4
Chauhan[58]	2015	Retrospective	4
Zevallos[59]	2016	Retrospective	4

* Holsinger et al[44] and Laccourreye et al[45] reported outcomes from the same study.

not satisfactory when compared with operation (five-year disease-specific survival was 47% in the operation group and 27% in the radiation group).[16]

In the same year, Perez et al reported long-term oncological outcomes (five and 10 years) of 32 years' experience (1959–1991) of radiotherapy alone, preoperatively, and postoperatively. They thought that radiotherapy was the treatment of choice in patients with stage T1–T2 carcinoma of the tonsillar fossa. In those with T3–T4 tumours who were in a good general condition, operation and postoperative irradiation offered better control than a single method of treatment and preoperative irradiation, but with greater morbidity. Complications in patients who had postoperative radiotherapy were severe dysphagia, oropharyngeal fistulas, and rupture of the carotid artery that resulted in death.[17]

More recently, a study of 53 patients treated between 1992 and 1998 for SCC of the base of the tongue, compared three different treatments: surgical resection combined with radiotherapy, radiotherapy alone, and radiotherapy plus interstitial radiation. Five-year survival and local control was lowest in patients treated with radiotherapy alone, but they had the best speech and swallowing outcomes.[25]

In a retrospective analysis of the surgical treatment of 87 patients with SCC of the base of the tongue in 2001, Gourin and Johnson[19] found that operation was effective for early disease. However, as a result of postoperative complications in those with advanced disease, they suggested organ-preserving protocols using radiotherapy or chemoradiation instead.

On the other hand, Galati et al[18] supported the use of operation for tonsillar SCC (even in patients with advanced lesions) to enable the biological staging of cancers that require adjuvant treatment. They emphasised the problems radiotherapy can cause (xerostomia, dysphagia, pain, difficulty in speaking, and dental caries), and the need for dental assessment before treatment to reduce the risk of osteoradionecrosis.

In their study of 18 patients (published in 2002) from Birmingham, UK, Watkinson et al supported combination treatment to improve five-year survival and quality of life in patients with T1 and T2 lesions.[22]

In 2003, Cosmidis et al[24] reported that operation alone had an essential role in patients with T1/T2, N0 disease, and they stated that the oncological results were similar to those of classic radiotherapy in terms of locoregional control and survival because it avoided the complications and aftereffects of radiotherapy. In cases of recurrence, they found that operations in non-irradiated areas resulted in lower morbidity and mortality. Postoperative radiotherapy could also be more effective.

To our knowledge, the first study that reported functional outcomes and quality of life (QoL) objectively after treatment of advanced SCC of the base of the tongue, was published in 2002. It included 61 patients (43 treated by operation and 18 by radiotherapy, with or without chemoradiotherapy or brachytherapy) with stage III and IV disease, and used three independent questionnaires. The first was the Performance Status Scale for Head and Neck Cancer Patients, which considered three areas of function: eating in public, understandability of speech, and normality of diet. The second was The University of Washington Quality of Life (UW-QoL) instrument, and the third, a questionnaire developed by the authors to evaluate the history of treatment. Statistical analysis showed that xerostomia was significantly worse with

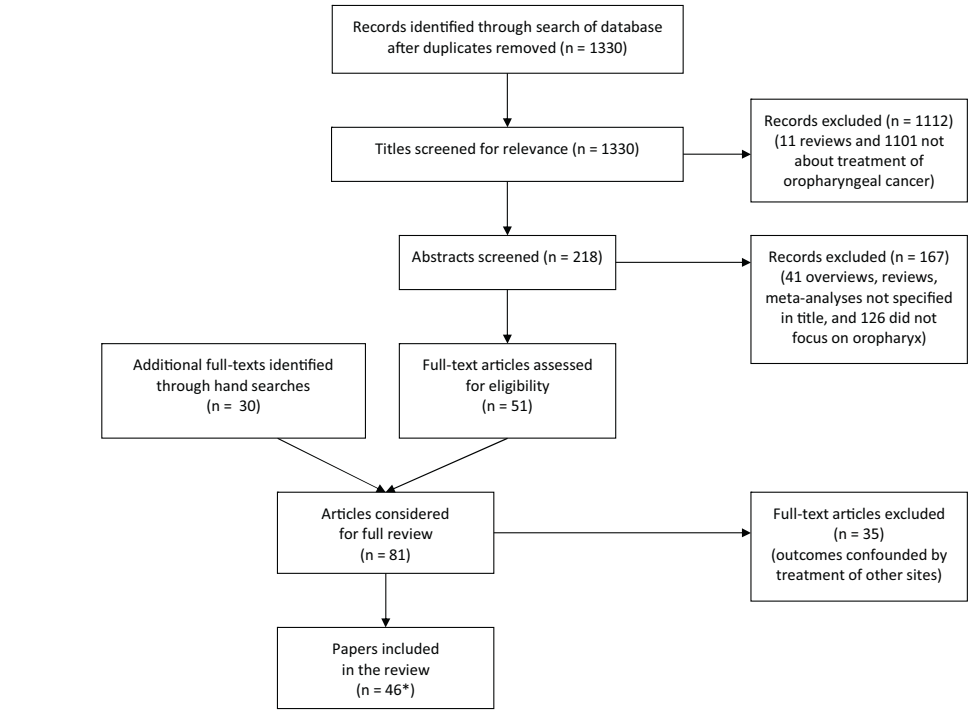

Fig. 1. Flow diagram of the search strategy.

Table 3
Questionnaires used.

Questionnaire and reference
Performance Status Scale for Head and Neck cancer Patients (PSSHN)[20,23,50]
University of Washington Quality of Life (UW-QoL)[20]
European Organisation for Research and Treatment of Cancer (EORTC) QLQ C30[21–23]
Head and Neck (H&N)35[21]
General Health Questionnaire (GHQ)12[22]
MD Anderson Dysphagia Inventory (MDADI)[40,48,54,56]
Head and Neck Cancer Inventory Health-Related Quality of Life (HNCI HRQoL)[37]
Short Form (SF) 8 Health Survey[50]
Voice Handicap Index (VHI)[54]

Table 4
Objective assessments used in the studies.

Objective assessment
Functional Outcome Swallowing Scale (FOSS)[46,47,49]
Communication Scale (CS)[46,47]
Normalcy of Diet Scale (subsection of the PSSHN)[56]
Weight loss[27,42]
Timed water swallowing test (WST)[56]
Duration of need for nasogastric tube[27,28,42–45,49,51–54,58]
Duration of need for tracheotomy[28,44,45,52]
Duration of hospital stay[44,45,49,52,53]
Readmission[59]

non-operative treatment, and that operation was associated with a longer hospital stay.[20]

Another study used two questionnaires, the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 core questionnaire and the specific head-and-neck cancer module (H&N35), to evaluate 113 patients two years after treatment for T1–T3 oropharyngeal SCC in two French cancer centres. Patients had brachytherapy with or without external beam radiotherapy, operation plus radiotherapy, or external beam radiotherapy only. The authors found that operation plus radiotherapy, as the initial treatment, favourably influenced scores for emotional function, but that brachytherapy had a negative influence on QoL.[21]

The first study we found that came to different conclusions in terms of functional outcome was done at the University Hospital of Geneva. The QoL of 60 patients had been assessed with the Performance Status Scale for Head and Neck Cancer Patients, and the EORTC QLQ-C30 questionnaire after radiotherapy with or without chemotherapy, or after radical surgery with or without radiotherapy. Functional outcomes for early disease were equivalent in the operation and radiotherapy groups, but in cases of advanced disease, the results were better in the radiotherapy group. As a result, the authors decided to move away from radical surgery to radical non-surgical treatment for all patients with advanced oropharyngeal cancers and, despite the ongoing movement in this direction, suggested that a prospective study with a larger sample size was essential.[23]

Conversely, in 2013, Iyer et al[30] reported successful five-year oncological outcomes in 128 patients who had primary conventional operations for T1/T2 SCC of the base of the tongue. The study period was from 1985 to 2005. Two

years later, the same team published a retrospective study of oropharyngeal SCC in patients who had primary operations with curative intent, and found that prognosis was better in those who were HPV-positive than in those who were not (five-year overall survival was 74% in the HPV-positive group and 44% in the HPV-negative group).[31]

Rodrigo et al reported good oncological and functional results at five years after a mandible-sparing approach using transhyoid surgery in patients with stages I, II, and III SCC of the base of the tongue.[29]

Diaz-Molina et al reported the results of conventional operations in patients with SCC of the lateral wall.[28] Intraoral, transpharyngeal, and transmandibular approaches, followed by radiotherapy in those with early and moderately advanced stages (I–III) resulted in good oncological and functional outcomes. In those with stage IV disease, morbidity was low and function preserved, but five-year oncological outcomes were poor, and patients were considered for concurrent chemoradiotheray.

Buiret et al[27] reported long-term functional outcomes (five and 10 years) in terms of alimentation in 254 patients who were treated surgically for oropharyngeal SCC (if operable) and radiotherapy with or without chemotherapy. To assess the impact of treatment on swallowing, the authors analysed the patients' weight, use of a nasogastric tube, and ability to eat solids, pastes, and liquids. Although 25.9% had surgical complications (infection, bleeding, pharyngostoma, cervical haematoma, pneumonia, orostoma, fever with an unknown cause, disunion of the flap, hepatic failure, acute delirium, and lymphorrhea), the authors stated that they preferred operation followed by radiotherapy to radiotherapy alone because of the potential long-term side effects of radiation (despite the lack of significant evidence).

In their study of 175 patients with recurrent tonsillar SCC after radical radiotherapy, Bachar et al[26] supported the use of operation when radiotherapy failed. They reported five-year overall survival of 23% and disease-free survival of 40%.

Organ-preservation

In 1996, Fein et al published the findings of 30 years' experience of the treatment of oropharyngeal SCC with radiotherapy alone at the primary site, with or without neck dissection. A total of 490 patients were treated between 1964 and 1991 with follow up of at least two years. Local control was achieved in 73% of patients with radiotherapy alone, overall local control after salvage was 78%, and 2.6% had severe complications (defined as those that required surgical intervention, inpatient stay, or resulted in death). The authors concluded that tumour control and survival after radiotherapy were comparable to the rates achieved with combined irradiation and operation, but with less morbidity.[32] Mendenhall et al[33] reached similar conclusions five years later. They reported good five-year oncological outcomes in their series of 400 patients treated for tonsillar SCC, and the incidence of severe complications was 5%.

In their comparison of organ-preservation and operation for advanced tonsillar SCC, Shirazi et al[35] found no significant difference in four-year overall survival and recurrence. The incidence of complications was similar in both groups: 26% after operation (serious wound infection, failed free flap, wound dehiscence, orocutaneous fistula) and 25% after organ-preservation treatment (haematological toxicity in those treated with chemotherapy, and xerostomia and osteonecrosis in those treated with radiotherapy). The authors therefore recommended organ-preservation treatment for patients with stage III–IV disease.

In 2004 the results were published of a French randomised prospective study that compared radiotherapy alone with concomitant chemoradiotherapy in patients with stages III and IV oropharyngeal SCC and no evidence of distant metastases. Five-year overall survival and locoregional control was better in the concomitant chemoradiotherapy group but there were more complications (56%) than in the radiotherapy group (30%). Anaemia was the most important prognostic factor for survival.[34]

Cartmill et al[40] reported ongoing problems with swallowing and salivary function two years after altered fractionation radiotherapy with concomitant boost (AFRT-CB). Patients' diets were restricted and they had not regained the weight they had lost.

The popularity of organ-preservation treatment grew after the introduction of IMRT, which improved locoregional control and survival when compared with conventional radiotherapy. These findings were published in a 2007 study that compared the three-year oncological outcomes of patients treated with IMRT with those treated before its introduction.[36] In 2010 Mendenhall et al[39] reported similar oncological results at five years in 130 patients. IMRT reduced the mean irradiation dose to the parotids and consequently the risk of long-term xerostomia.

Yao et al[37] compared the health-related quality of life (HRQoL) of patients who had IMRT with that of those who had conventional radiotherapy. At 12 months, eating, speech, aesthetics, and social disruption, were better in the IMRT group than in the radiotherapy group. However, at three months, both groups had a considerable reduction in the eating domain, and at six months, function had started to improve in the IMRT group, but was continuing to deteriorate in the other.

In comparison with 3-dimensional conformal radiotherapy (3D-RT) and accelerated fractionation with concomitant boost (AFxCB), IMRT was more effective and resulted in less skin and mucosal toxicity in patients treated for stage III and IV oropharyngeal SCC.[38]

Lohia et al[42] found that when compared with 3-dimensional conformal radiotherapy, IMRT improved outcomes related to toxicity (effect on skin and mucous membranes) and the need for a percutaneous endoscopic gastrostomy (PEG) tube.

Self et al[41] studied the risk of oropharyngeal haemorrhage, a life-threatening complication associated with chemora-

diotherapy alone. The most important determinant for its occurrence was advanced T stage (nodal disease was not a risk factor), and it occurred in patients with recurrent or persistent disease, or both, or those with radiation necrosis.

Different combinations of chemoradiotherapy have been used to minimise morbidity without compromising the oncological results. Dobrosotskaya et al[43] found that in locally advanced SCC, three-year survival in patients treated weekly with chemotherapy plus radiotherapy was similar to that in those treated with high-dose chemotherapy plus radiotherapy, but was better tolerated.

Minimally-invasive surgery

A prospective study published in 2006 by Grant et al[46] presented the functional and oncological outcomes of all patients treated with transoral microsurgery for SCC of the base of the tongue (1997–2005) at the Mayo Clinics in Jacksonville, Florida, and Scottsdale, Arizona. The authors concluded that it was a promising alternative to conventional surgery, with or without radiotherapy, and resulted in favourable local control and survival, with fewer functional side-effects.

Seven years later, in a similar study on SCC of the base of the tongue, Canis et al[51] came to a similar conclusion about the effectiveness of primary transoral microsurgery, but they had combined it with radiotherapy with or without chemotherapy.

Holsinger et al[44] and Laccourreye et al[45] reported the use of transoral lateral oropharyngectomy as a conservative alternative to radiation therapy. These two studies reported 20 years' retrospective analysis of the same 191 patients, and stated that the approach, which allowed en bloc resection of the mucosa and muscle through a non-invaded peripharyngeal space, could be used safely in patients with T1 or T2 SCC of the tonsil without posterior anatomical spread. The authors thought that it was oncologically superior to direct transoral resection with the superior constrictor at the deep margin, as described by Galati et al,[18] and piecemeal resection as described by Watkinson et al.[22] They reported an incidence of complications of 6.3%, and good functional and oncological outcomes that were comparable to radiotherapy.[44,45]

In a United States multicentre prospective study of the functional and oncological outcomes of 204 patients with advanced oropharyngeal SCC, Haughey et al[49] found that transoral microsurgery was a highly effective primary treatment, particularly in those with HPV. They found that, although adjuvant treatment improved survival and local control, the addition of chemotherapy was not associated with significantly better oncological outcomes when compared with radiotherapy alone. The good functional and oncological outcomes offered by this approach were also noted by Chauhan et al[58] in a minor single-centre Irish study.

Moore et al[47] reported good preliminary functional outcomes in 45 patients treated by TORS for oropharyngeal SCC. Function was evaluated four weeks after operation or three months after completion of radiotherapy or chemotherapy. The mean (range) follow up of 12.3 (1–16) months was insufficient to show adequate oncological control, but functional results were promising. Speech was normal in all patients postoperatively and there were no life-threatening complications. Orocutaneous fistulas developed in three.

Leonhardt et al[50] used two questionnaires to evaluate QoL one year after treatment. They found that TORS plus radiotherapy resulted in better functional outcomes than TORS plus chemoradiotherapy. According to Dziegielewski et al,[53] speech was only moderately affected by TORS.

Sinclair et al[48] used the MD Anderson Dysphagia Inventory (MDADI) to objectively assess patient-perceived dysphagia in 42 patients treated by TORS and adjuvant radiotherapy and chemoradiotherapy for T1 or T2 disease. One third reported a reduction in swallowing function that improved over the time. Adjuvant chemotherapy required prolonged dependence on a gastrostomy tube.

Lee et al[54] compared TORS with conventional surgery through a transoral approach or mandibulotomy for tonsillar SCC. They used the Voice Handicap Index, the MD Anderson Dysphagia Inventory, and dependence on nasogastric feeding, to show the better functional outcomes achieved with TORS. Complications occurred only in the mandibulotomy group (one flap revision, one malunion, and one case of osteoradionecrosis).

Ford et al[55] confirmed that survival at three years after TORS was better than that after open operation (89% compared with 73%, respectively). They found that oncological outcomes after a combination of treatments were better in patients with HPV.

In a retrospective matched study on salvage surgery, White et al[52] compared TORS with open surgical approaches and recorded operative (blood loss, operating time, status of the margins, and complications) and functional (duration of hospital stay, use of a tracheostomy, and use of a feeding tube) outcomes. Generally, patients treated by TORS lost 6.7 times less blood, operations were shorter by about one third, and the hospital stay was reduced by 50%. Outcomes for speech and swallowing, and two-year survival, were considerably better in the TORS group (74% compared with 43%, respectively). More margins were invaded in the open operation group. The incidence of final invaded margins in the TORS group was lowered by further resection in outpatients. This would not have been possible in the open operation group.

Zevallos et al,[59] who based their study on the American National Cancer Database, compared the perioperative outcomes of TORS with the non-robotic transoral approaches used between 2010 and 2011 in 514 patients with oropharyngeal SCC. The primary outcome measure was the final report on the surgical margin, and secondary outcomes were duration of hospital stay, rates of conversion to open operation, 30-day unplanned readmissions, and 30-day mortality. Patients treated by TORS had significantly lower rates of invaded margins than those treated by non-robotic transoral surgery. Rates for conversion to open surgery

were higher in the non-robotic group than in the TORS group. Overall rates of unplanned readmissions were 3.1% and the difference between the groups was not significant. The results of the study suggested that the selection of patients and the surgeon's experience were more important predictors of negative margins than the type of transoral approach.

Smith et al compared the outcomes of TORS with primary chemoradiotherapy in a prospective non-randomised study that was matched for tumour stage. Results showed a survival benefit in the TORS group with three-year overall survival of 83% compared with 57%, and disease-specific survival of 94% compared with 85%. The authors found that primary surgical management of oropharyngeal SCC with TORS together with neck dissection provided accurate staging of patients in case of the need for further treatment.[57]

O'Hara et al[56] concluded that primary transoral laser microsurgery affected swallowing less than primary chemoradiotherapy even in cases of stage III and IV oropharyngeal SCC. Their study used the MD Anderson Dysphagia Inventory, the Performance Status Scale, and a timed water swallow test to analyse functional outcomes before, and three months after, treatment.

Complications

The complications reported in the studies are presented in Table 5.

Discussion

Histologically, the oropharynx is a distinct anatomical entity with a discontinuous basement membrane. HPV directly involves the immune system, and a patient's status in this regard influences and modifies the behaviour of oropharyngeal SCC.[6,7] HPV vaccination seems to reduce the prevalence of HPV, but we know of no trials to validate the effect of vaccination to prevent infection and HPV-positive oropharyngeal SCC.[61] Local infiltration of immune cells and innate systemic inflammation have already been studied in this disease.[62,63] Immunotherapy will probably be the subject of future studies, but as yet, these findings have had no impact on current treatments.

The purpose of this review was to show how treatments have evolved in the last 25 years and to assess how accurately we can recommend a treatment in a multidisciplinary team meeting.

Although the studies reflect the developments in clinical practice, most of them reported series without randomisation so the choice of treatment was based on personal preference. The differences in the treatments and functional outcome measures made comparison difficult, and the low level of evidence for the decisions made reflects the lack of certainty about which would be best.

All health professionals who treat patients with cancer of the head and neck will have seen the transition from conventional primary surgery to organ-preservation treatment after publication of the preliminary results of the Veterans Affairs

Table 5
Overall complications by type of treatment.

Conventional surgery	Chemoradiotherapy	Minimally-invasive surgery
Wound infections[14,15,27,28,29,35]	Dysphagia[14,18,32,33,36,40]	Pulmonary compromise/aspiration pneumonia[44,45,51]
Fistula/pharyngostoma/orostoma[14,15,19,27,35]	Xerostomia[18,36,38,39,40,47]	Rhinolalia[44,45]
Partial flap necrosis/flap disunion[14,27]	Difficulty speaking[18]	Chyle leak[44,45]
Pulmonary compromise/aspiration pneumonia[14,19,28,29]	Stiff neck[40]	Seroma[44,45]
Upper airway oedema[19]	Loss of appetite[40]	Cervical abscess/sepsis[44,45]
Malocclusion[15]	Agneusia[34]	Wound breakdown[58]
Fatal rupture of carotid artery in salvage operation[17]	Dental caries[18,36]	Cerebrovascular event[44,45]
Temporary dysphagia[18]	Aspiration pneumonia[32,33]	Dysphagia[44,45,51]
Temporary paresis of hypoglossal nerve[19]	Skin toxicity[32,40,42,43]	Postoperative bleeding/cervical haematoma[44,45,46,49,51,53,57,58]
Paralysis of phrenic nerve[19]	Mucosal toxicity[32,40,42,43]	Orocutaneous fistula[47,53,58]
Pneumointestinalis coli[19]	Facial oedema[36]	Trismus[47]
Postoperative haemorrhage/haematoma[27,29,52]	Oesophageal stenosis[49]	Oral ulceration[47]
Seroma[29]	Tracheal fibrosis[36]	Shoulder pain[47]
Chyle leak[27]	Laryngeal necrosis[32]	Paresis of hypoglossal nerve[49]
Hepatic failure[27]	Necrosis of the pharynx and parapharyngeal space[49]	Velopharyngeal incompetence [49]
Acute delirium[27]	Osteonecrosis[18,19,32,36,33,39]	
	Neurological toxicity[34,43]	
	Ototoxicity[34]	
	Gastrointestinal toxicity[43]	
	Weight loss[34,42]	
	Haematological toxicity [34,43]	
	Haemorrhage[41]	
	Fatigue/weakness[43]	

Study[11] in 1991, which was based on the management of laryngeal SCC.[64,65]

We included studies that were published after 1992. Cohort studies after 2000 showed that operation alone was no longer an option, as the paradigm had shifted in favour of primary radiotherapy alone or with chemotherapy.

Organ-preservation treatment based on chemoradiotherapy avoided the surgical complications that were mainly the result of invasive approaches (Table 5). Most occurred immediately postoperatively (pulmonary compromise, infection, formation of a fistula, failure of the flap) and a higher incidence of those that were fatal were seen in patients who had had preoperative radiotherapy and needed salvage surgery. The complications after salvage surgery were breakdown of the wound, orocutaneous fistula, fatal rupture of the subclavian artery, and mandibular fracture. The blame should be placed largely on radiation.[17]

As the success of radiotherapy began to be seen, its complications also became evident. The most common was xerostomia, which reduced patients' QoL. A combination of chemotherapy and radiotherapy improved oncological outcomes but increased the complications, and a French study, the only randomised trial we found, [34] showed that late toxicity was more common after chemoradiotherapy than after radiotherapy alone (56% compared with 30%, respectively).

Compared with operation, the adverse effects of chemoradiotherapy were more silent, and toxicity, such as osteonecrosis, stenosis, and fibrosis, appeared late and were difficult to treat (Table 5). IMRT seemed to reduce xerostomia more than classic radiotherapy[38] and, compared with conventional chemoradiotherapy, also improved overall survival[36] and QoL.[37]

We included two studies by Mendenhall et al that were published 10 years apart (2000 and 2010). The first reported treatment with conventional radiotherapy[33] and the second with IMRT.[39] Although lower doses to the salivary glands with IMRT reduced xerostomia, the authors still reported osteonecrosis that required segmental mandibulectomy, as well as soft tissue necrosis and haemorrhage.

Iyer et al[31] showed that surgical outcomes were better in HPV-positive patients, and this group also responded better to chemoradiotherapy.[43] One should, however, question whether there are two types of disease: HPV-positive and HPV-negative. Viral infections affect the immune system, and the good response in younger patients with HPV supports this hypothesis.

Minimally-invasive techniques have developed exponentially over the last decade.

The complications related to transoral microsurgery were not as severe as those for conventional operations (Table 5), but adjuvant treatment increased the number that were serious. These included late-radiation-induced oesophageal stenosis, and necrosis of the pharynx and parapharyngeal space,[49] to name but a few. Long-term dependence on percutaneous feeding (PEG) has been seen in patients who had adjuvant radiotherapy,[46] and late-onset muscular fibrosis can cause difficulty in swallowing.

Operations that cause no neurological trauma and leave the anatomy intact may have better outcomes than organ-preservation treatment with its associated complications. Two randomised controlled trials are currently comparing minimally invasive surgery with radiotherapy or chemotherapy. The first, a phase II trial, is comparing primary radiotherapy with TORS (ORATOR) for small-volume primary T1, T2, N0-2, early-stage SCC of the oropharynx. The second is the European Organisation for Research and Treatment of Cancer 1420 (EORTC 1420-HNCG-ROG), which is a phase III randomised controlled trial to assess the best of radiotherapy with TORS/transoral microsurgery in patients with T1, T2, N0 disease.[66] The results, which are expected in 2021, should provide better evidence on the treatment of early-stage disease, but more work is needed to inform the management of more advanced cancers.

A patient's suitability is dictated by any coexisting conditions and their ability to cope with the treatment. Cancers of the head and neck are multifactorial diseases that behave differently within the oropharynx. Their pathophysiological behaviour also seems to vary between patients who have, and do not have, HPV.

To summarise, we are still far away from being able to recommend the best treatment, but we have raised questions as to the possibility of two distinct entities within oropharyngeal SCC. We have also identified the immediate and late complications reported during the era of conventional surgery, focused on the evidence for late toxicity after organ preservation treatment and chemoradiotherapy, and reported some encouraging results with the use of the latest technologies.

Conflict of interest

We have no conflicts of interest.

Ethics statement/confirmation of patients' permission

Ethics approval not required. Patients' permission not applicable.

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