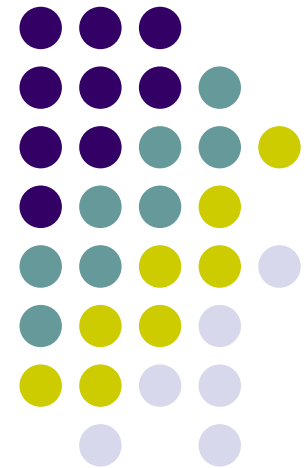


Evidence-Based Medicine conference

Present by R1 詹文祥
指導老師：李家和 醫師



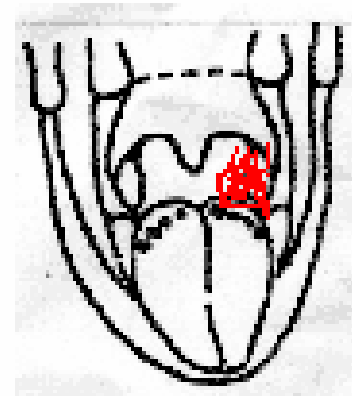
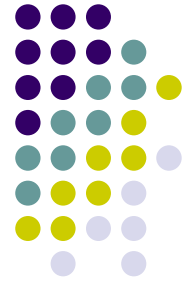
個案病歷摘要



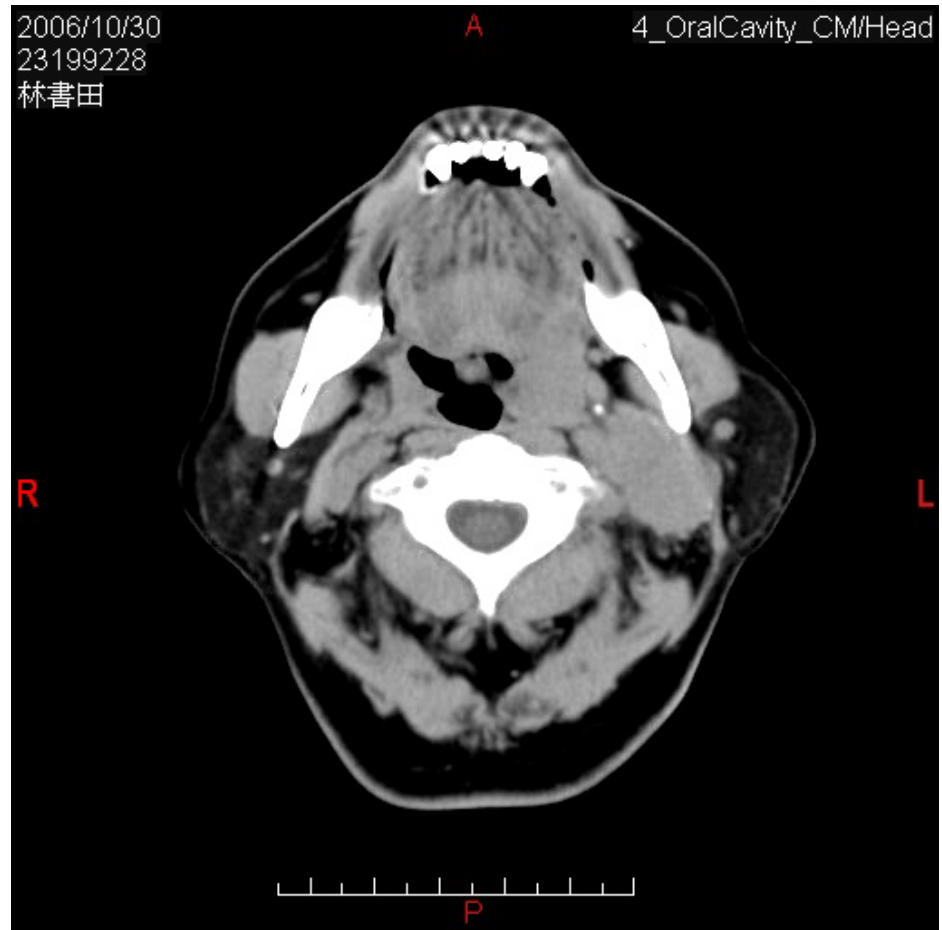
- C.C.: A left neck mass noted for 1+ month.
- P.I.:

This 62 year-old male patient is quite well-being before. According to his statement, a left neck mass was noted for about 1+ month. Body weight loss(3kg/month) was also noted. As a result, he went to our OPD for help, and bulging of his left tonsil was found. The character of his left neck mass: 3 x 3 cm, fixed, non-tender. Biopsy of left tonsil was performed and it revealed SCC. The other associated s/s: oral bleeding(-), sore-throat(-), odynophagia(-), dysphagia(-). Under the impression of tonsillar cancer with neck metastasis, he is admitted to our ward for further evaluation and chemotherapy.

Local findings



CT





Pathology

- 組織名稱：Tonsil.
- 臨床診斷：Tonsillar ca with neck metastasis.
- 收件日：951031
- 病理診斷：
Oral cavity, tonsil, left, biopsy, squamous cell carcinoma, grade II.

Impression

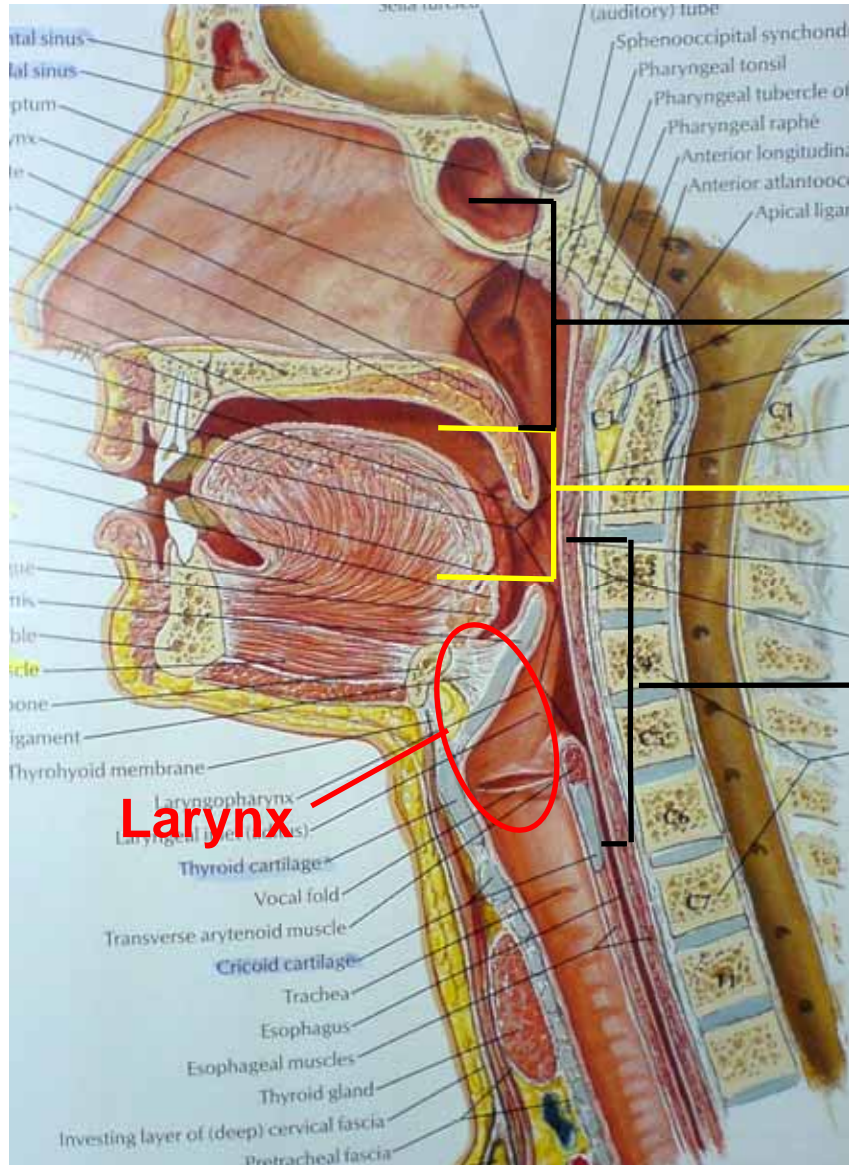
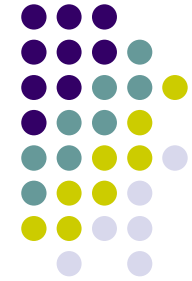
- Tonsillar cancer with neck metastasis
(T1N1M0, stage III)





- What can we do for this patient?

Background information



Nasopharynx

Nasal cavity後面, above soft palate

Oropharynx

Below soft palate, Tonsils 到vallecula (tongue base and epiglottis之間的凹陷)

Hypopharynx

Epiglottis上緣到 cricoid cartilage下緣

Larynx

All illustrations are adapted from F. H. Netter



Background information

- Head & neck surgery – Otolaryngology, 4th edition:

Patients with advanced disease treated with **surgery and postoperative radiotherapy** can be expected to have approximately a **50% 3-year survival** and **greater than 70% local control rate**.

The results are **very similar** with **concurrent chemoradiation**.

Asking

- Which kind of treatment is better for advanced oropharyngeal cancer?





PICO

提出可回答的臨床問題(Asking)

P: Patient with advanced oropharyngeal cancer

I: concurrent chemoradiation therapy

C: Surgery

O: Compare the prognosis of surgery and concurrent chemoradiation therapy



Acquire

- Key word: oropharyngeal cancer
Tonsillar cancer
- Reference database :
 - (1) Cochrane Database of Systematic Reviews
 - (2) The Cochrane Library
 - (3) PubMed Medline-Systematic Reviews
 - (4) PubMed- by Clinical Study Category
 - (5) MeSH database

Searching.....

Cochrane Database of Systematic Reviews



EBM Reviews - Cochrane Database of Systematic Reviews
<4th Quarter 2003>

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1	oropharyngeal cancer.mp. [mp=title, short title, abstract, full text, keywords, caption text]	0	-
2	oropharynx cancer.mp. [mp=title, short title, abstract, full text, keywords, caption text]	0	-
3	(head and neck cancer).mp. [mp=title, short title, abstract, full text, keywords, caption text]	8	Display

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- **Cochrane Database of Systematic Reviews**
- **Search terms**
 - (1) **Oropharyngeal cancer → 0**
 - (2) **Head and neck cancer → 8 → 0**

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The Cochrane Library



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Chemotherapy added to locoregional treatment for head and neck squamous-cell carcinoma: three meta-analyses of updated individual data (Structured abstract)
Centre for Reviews and Dissemination
Original Author(s): J P Pignon, J Bourhis, C Domenge, L Designe
Year: 2004
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- The Cochrane Library
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Items 1 - 36 of 36 One page.

- 1: [Chen AY, Schrag N, Hao Y, Stewart A, Ward E.](#) Related Articles, Links
Changes in treatment of advanced oropharyngeal cancer, 1985-2001.
Laryngoscope. 2007 Jan;117(1):16-21.
PMID: 17202924 [PubMed - in process]
- 2: [Dewil B, Jorissen M, Lemkens P.](#) Related Articles, Links
Routine pathological evaluation after tonsillectomy: is it necessary?
B-ENT. 2006;2(3):103-8.
PMID: 17067078 [PubMed - indexed for MEDLINE]
- 3: [Hobbs CG, Sterne JA, Bailey M, Heyderman RS, Birchall MA, Thomas SJ.](#) Related Articles, Links
Human papillomavirus and head and neck cancer: a systematic review and meta-analysis.
Clin Otolaryngol. 2006 Aug;31(4):259-66. Review.
PMID: 16911640 [PubMed - indexed for MEDLINE]
- 4: [Taylor B, Rehm J, Gmel G.](#) Related Articles, Links
Moderate alcohol consumption and the gastrointestinal tract.
Dig Dis. 2005;23(3-4):170-6. Review.
PMID: 16508280 [PubMed - indexed for MEDLINE]

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- PubMed Medline-Systematic Reviews
- Search term
Oropharyngeal cancer → 1/36



- Changes in treatment of advanced oropharyngeal cancer, 1985-2001. Laryngoscope. 2007 Jan;117(1):16-21. PMID: 17202924

Changes in treatment of advanced oropharyngeal cancer, 1985-2001



- [Chen AY, Schrag N, Hao Y, Stewart A, Ward E. Related Articles,](#)
- Laryngoscope. 2007 Jan;117(1):16-21.
- PMID: 17202924
- Level: 4 (Case-series)
- Method: We extracted oropharyngeal squamous cell cancer cases from the [National Cancer Database](#). Type of initial treatment, type of facility, stage of tumor, payer status, and demographic variables were collected.
- A total of [54,801 cases](#) of oropharyngeal cancer meeting the inclusion criteria were available for analysis during the time period [1985 to 2001](#).



- Discussion:
 - (1) Information from clinical trials on oropharyngeal cancer treatment is **very limited**.
 - (2) **No trial has been published that compared locoregional control and survival for patients treated with chemo-RT versus surgery.**
 - (3) It is nonetheless generally agreed that **chemo-RT** is superior to RT alone.

Searching.....

PubMed- by Clinical Study Category



PubMed Clinical Queries - Microsoft Internet Explorer

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- 1: [Fallai C, Bolner A, Signor M, Gava A, Franchin G, Ponticelli P, Taino R, Rossi F, Ardizzoia A, Oggionni M, Crispino S, Olmi P.](#) Related Articles, Links
Long-term results of conventional radiotherapy versus accelerated hyperfractionated radiotherapy versus concomitant radiotherapy and chemotherapy in locoregionally advanced carcinoma of the oropharynx. *Tumori*. 2006 Jan-Feb;92(1):41-54. PMID: 16683383 [PubMed - indexed for MEDLINE]
- 2: [Ozer E, Grecula JC, Agrawal A, Rhoades CA, Young DC, Schuller DE.](#) Related Articles, Links
Long-term results of a multimodal intensification regimen for previously untreated advanced resectable squamous cell cancer of the oral cavity, oropharynx, or hypopharynx. *Laryngoscope*. 2006 Apr;116(4):607-12. PMID: 16585867 [PubMed - indexed for MEDLINE]
- 3: [Semrau R, Mueller RP, Stuetzer H, Staar S, Schroeder U, Guntinas-Lichius O, Kocher M, Eich HT, Dietz A, Flentje M, Rudat V, Volling P, Schroeder M, Eckel HE.](#) Related Articles, Links
Efficacy of intensified hyperfractionated and accelerated radiotherapy and concurrent chemotherapy with carboplatin and 5-fluorouracil: updated results of a randomized multicentric trial in advanced head-and-neck cancer. *Int J Radiat Oncol Biol Phys*. 2006 Apr 1;64(5):1308-16. Epub 2006 Feb 7. PMID: 16464538 [PubMed - indexed for MEDLINE]

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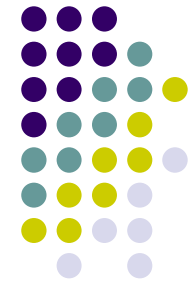
- PubMed- by Clinical Study Category
- Search term
Oropharyngeal neoplasm(therapy)

→ **2/70**



- Inoperable oropharyngeal carcinoma treated with concomitant irradiation, mitomycin C and bleomycin - long term results.
Neoplasma. 2005;52(2):165-74.
PMID: 15800716
- Concomitant radiochemotherapy with cisplatin (CDDP), 5-fluorouracil (5-FU) and mitomycin C (MMC) in locally advanced carcinoma of the oropharynx. Results of a phase II trial]
Bull Cancer. 1995 Dec;82(12):1044-51. Review.
French.
PMID: 8745671

Inoperable oropharyngeal carcinoma treated with concomitant irradiation, mitomycin C and bleomycin - long term results.



- Neoplasma. 2005;52(2):165-74.
- Level: 1b (prospective randomized clinical trial)
- Methods: Patients with inoperable head and neck tumors were treated concomitantly with radiochemotherapy with mitomycin C and bleomycin in our prospective randomized clinical trial (1991- 1993).
- Ninety-five patients with stage III and IV inoperable oropharyngeal squamous cell carcinoma were treated with curative intent, concomitantly with supra-voltage irradiation 2 Gy/day 5 times weekly to 60-73 Gy, bleomycin 5 mg 2 times weekly and. one application of mitomycin C 15 mg/m² after 10 Gy.
- Median follow-up was 85 months.



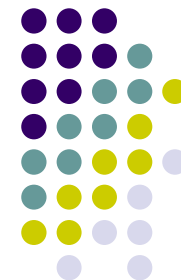
- Results:

The **loco-regional control, disease-free survival** and **overall survival at 5 years** were **55%** , **51%** and **32%** (95% CI: 44-67%, 41-62%, 22-42%), respectively.

Concomitant radiochemotherapy with cisplatin (CDDP), 5-fluorouracil (5-FU) and mitomycin C (MMC) in locally advanced carcinoma of the oropharynx. Results of a phase II trial]



- Bull Cancer. 1995 Dec;82(12):1044-51.
- Level: 2b (low quality RCT)
- Method: phase II trial was designed to establish the feasibility of concomitant conventional radiotherapy and three cycles of chemotherapy at day 1, 21 and 42 with cisplatin (CDDP) 20 mg/m² and 5-fluorouracil (5-FU) 400 mg/m² day 1 to day 4, and mitomycin C (MMC) 10 mg/m² day 1.
- From March 1990 to September 1993, 27 patients (mean age: 55) were included in this study. Three patients (11%) were T2N0, 19 (70%) T3 (T3N0: n = 9, T3N1: n = 1, T3N2: n = 5, T3N3: n = 4), and 5 (19%) T4 (T4N0: n = 1, T4N1: n = 1, T4N2: n = 2, T4N3: n = 1).



- With a mean follow-up of 34 months
- Results:
 - (1) One and 2-year overall survival rates were 68 and 61%
 - (2) A high complete response rate has been achieved with this concomitant radio-polychemotherapy, but with a severe digestive and haematological toxicity, which did not allow to conclude to the feasibility of this therapeutic association.

Searching..... MeSH database



The screenshot shows the MeSH (Medical Subject Headings) database search interface. The browser window title is "MeSH - Medical Subject Headings - Microsoft Internet Explorer". The search bar contains "MeSH" and "for Tonsillar cancer". The search results show one result: "1: Tonsillar Neoplasms". The interface includes a navigation menu on the left, a search bar at the top, and a list of subheadings for the selected term. The subheadings are listed with checkboxes, and "therapy" is checked.

MeSH - Medical Subject Headings - Microsoft Internet Explorer

NCBI MeSH A service of the National Library of Medicine and the National Institutes of Health

Search MeSH for Tonsillar cancer

Suggestions: Tonsillar cancer; Tonsillar cancers; Cancer, tonsillar; Cancers, tonsillar; Tonsil cancers; Tonsil cancer; Cancers, tonsil; Testicular cancer; Cerebellar cancer; Cancer, tonsil; more...

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- If making selections (e.g., Subheadings, etc.), use the [Send to Search Box](#) feature to see PubMed records with those specifications.
- Select PubMed under the Links menu to retrieve all records for the MeSH Term.
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1: Tonsillar Neoplasms
Tumors or cancer of the TONSIL.

[Subheadings:](#) This list includes those paired at least once with this heading in MEDLINE and may not reflect current rules for allowable combinations.

- analysis
- blood
- blood supply
- chemically induced
- chemistry
- classification
- complications
- congenital
- diagnosis
- drug therapy
- economics
- enzymology
- epidemiology
- ethnology
- etiology
- genetics
- history
- immunology
- metabolism
- microbiology
- mortality
- nursing
- pathology
- physiopathology
- prevention and control
- radiation effects
- radiography
- radionuclide imaging
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- rehabilitation
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- secretion
- surgery
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Limits: English, published in the last 5 years, Humans

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- 1: [Charbonneau N, Gelinas M, del Vecchio P, Guertin L, Larochelle D, Tabet JC, Soulieres D, Charpentier D, Nguyen-Tan PF.](#) Related Articles, Links
Primary radiotherapy for tonsillar carcinoma: a good alternative to a surgical approach.
J Otolaryngol. 2006 Aug;35(4):227-34.
PMID: 17176797 [PubMed - indexed for MEDLINE]
- 2: [Pakos EE, Tsekeris PG, Gogou PV, Koutis EV, Capizzello A, Exarchakos G.](#) Related Articles, Links
Cutaneous melanoma with tonsillar metastasis.
Tumori. 2006 Sep-Oct;92(5):437-9. Review.
PMID: 17168439 [PubMed - indexed for MEDLINE]
- 3: [Laccourreye O, Menard M, Behm E, Garcia D, Cauchois R, Holsinger FC.](#) Related Articles, Links
Sternocleidomastoid myofascial flap for reconstruction after composite resection of invasive squamous cell carcinoma of the tonsillar region: technique and outcome.
Laryngoscope. 2006 Nov;116(11):2001-6.
PMID: 17075422 [PubMed - indexed for MEDLINE]

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- MeSH database
- Limits: English, published in the last 5 years, Humans
- Search term
"Tonsillar Neoplasms/therapy"[MeSH]
→ 2/99



- Current management of tonsillar cancer.
Oral Oncol. 2003 Jun;39(4):337-42. Review.
PMID: 12676252
- Advanced-staged tonsillar squamous carcinoma: organ preservation versus surgical management of the primary site.
Head Neck. 2006 Jul;28(7):587-94.
PMID: 16475199

Current management of tonsillar cancer.



- Oral Oncol. 2003 Jun;39(4):337-42. Review.
- Level: 3a
- In contrast to early tonsillar disease, advanced tonsil cancer represents a clinical challenge that requires multimodality therapy.
- While advanced lesions are often treated with a combination of radiation, chemotherapy, and surgical ablation, management of the neck and distant metastases continues to present a therapeutic dilemma.

Advanced-staged tonsillar squamous carcinoma: organ preservation versus surgical management of the primary site.



- Head Neck. 2006 Jul;28(7):587-94.
- Level: 3b (case-control)
- METHODS: The records of 74 patients with advanced-stage tonsillar SCC were reviewed. The median age at diagnosis was 58 years. Thirty-eight patients received definitive surgery to the primary site, and 36 were treated with an organ-preservation approach (OP) using radiotherapy +/- chemotherapy.
- RESULTS: No significant difference in overall survival (OS) or freedom from relapse (FFR) by treatment was found.



- **CONCLUSION:** Patients treated with OP and primary surgery had **comparable** OS and FFR. T classification and N status were significant independent predictors for tumor relapse and survival. On the basis of these results, we **favor organ-preservation therapy** for patients with advanced-stage tonsillar SCC.

Table 3. Local and regional control, freedom from relapse, and overall survival by treatment group.

	Surgery, %	Organ preservation, %	<i>p</i> value
4-y local control	94	86	.29
4-y regional control	87	92	.58
4-y freedom-from-relapse	67	53	.39
4-y overall survival	71	48	.27

Searching.....



- MeSH database
- Search term: Oropharyngeal cancer
("Oropharyngeal Neoplasms/radiography"[MeSH] OR
"Oropharyngeal Neoplasms/surgery"[MeSH] OR "Oropharyngeal
Neoplasms/therapy"[MeSH])
- Limits: published in the last 5 years, Clinical Trial, Meta-Analysis,
Randomized Controlled Trial, Review
→ 1/102



- Organ preservation therapy using induction plus concurrent chemoradiation for advanced resectable oropharyngeal carcinoma: a University of Pennsylvania Phase II Trial.
J Clin Oncol. 2002 Oct 1;20(19):3964-71.
PMID: 12351593

Organ preservation therapy using induction plus concurrent chemoradiation for advanced resectable oropharyngeal carcinoma: a University of Pennsylvania Phase II Trial.



- J Clin Oncol. 2002 Oct 1;20(19):3964-71.
- Level: 2b (Low-quality RCT)
- PATIENTS AND METHODS: Patients had technically resectable stage III/IV squamous cell carcinoma of the oropharynx, exclusive of T1-2N1. Induction chemotherapy consisted of carboplatin (area under the curve formula equal to 6) and paclitaxel 200 mg/m² for two cycles, followed by re-evaluation. Patients with major response continued to definitive radiotherapy (70 Gy over 7 weeks) plus concurrent once-weekly paclitaxel (30 mg/m²/wk). Patients with advanced neck disease also underwent post-radiation therapy neck dissection and two more chemotherapy cycles.



- RESULTS: Fifty-three patients were enrolled. Median follow-up was 31 months (minimum follow-up for survivors was 18 months). The major response rate to induction chemotherapy was 89%; 90% of patients had a complete response after concurrent chemoradiation. Actuarial survival at 3 years was 70%, and 3-year event-free survival was 59%. The 3-year actuarial locoregional control was 82% and the 3-year actuarial rate of distant metastases was 19%.

Searching.....



- PubMed
- Limits: English, published in the last 5 years, Clinical Trial, Meta-Analysis, Practice Guideline, Randomized Controlled Trial, Review, Humans, Core clinical journals, Cancer
- Search terms
Oropharyngeal cancer
→3/129



- Concurrent chemoradiation for locally advanced oropharyngeal cancer.
Am J Otolaryngol. 2007 Jan-Feb;28(1):3-8.
PMID: 17162122
- Treatment of advanced oropharyngeal cancers with chemotherapy and radiation.
Ear Nose Throat J. 2003 May;82(5):367-70.
PMID: 12789762
- Current management of tonsillar cancer.
Oral Oncol. 2003 Jun;39(4):337-42. Review.
PMID: 12676252

Concurrent chemoradiation for locally advanced oropharyngeal cancer.



- Am J Otolaryngol. 2007 Jan-Feb;28(1):3-8.
- Level: 4 (case-series)
- MATERIALS AND METHODS: A retrospective survey of patients who underwent chemotherapy and radiation for locally advanced oropharyngeal carcinoma at the Veteran Affairs North Texas Health Care System, Dallas, Tex.
- Results:
 - (1) At a median follow-up of 23 months, the 3- and 5-year survival for the whole group were, respectively, 52% and 41%.
 - (2) The 5-year survival for T1-T2 and T3-T4 tumors was, respectively, 84% and 27%



- CONCLUSION: Concurrent chemoradiation provided **good locoregional control** for locally advanced oropharyngeal carcinoma. Patients with small tumors (T1-T2) had excellent survival. The **poor prognosis** associated with **large tumors** may be due to the risk of developing distant metastases.

Treatment of advanced oropharyngeal cancers with chemotherapy and radiation.



- Ear Nose Throat J. 2003 May;82(5):367-70.
- Level: 4 (case-series)
- Method:a retrospective chart review of treatment outcomes in 17 adults who had been selected to undergo concomitant chemotherapy and radiation (chemo/XRT) for late-stage oropharyngeal cancers.



In a series of patients with cancer of the base of the tongue, Gourin and Johnson found that overall control rates following surgery with postoperative radiation ranged from 72 to 92%.⁵ In a study of patients with oropharyngeal cancers, Zelefsky et al reported an overall 7-year survival rate of 52% and a disease-free control rate of 64%.⁶ In patients with stage IV cancers of the head and neck following chemo/XRT, Vokes et al found that the locoregional control rate was 92% and overall survival was 55% (median follow-up: 38 mo).⁷ Calais et al reported a 3-year survival rate of 42% among patients with oropharyngeal cancers in the chemo/XRT arm of their study.⁸ Nathu et al found a 63% local control rate for oropharyngeal cancers after 5 years.⁹ Poole et al demonstrated local control rates of 71 and 60% in primary oropharyngeal tumors and cervical node metastases, respectively.¹⁰



- Conclusion

Our data suggest that patients with advanced-stage oropharyngeal cancers should be offered the option of being treated with chemo/XRT. In our small series, loco-regional control rates following chemo/XRT were similar to those that have been reported following surgery with postoperative radiation. In addition, organ preservation was achieved with an acceptable degree of morbidity.

Appraisal



Level	Therapy/Prevention, Aetiology/Harm
1a	SR (with homogeneity*) of RCTs
1b	Individual RCT (with narrow Confidence Interval‡)
1c	All or none§
2a	SR (with homogeneity*) of cohort studies
2b	Individual cohort study (including low quality RCT; e.g., <80% follow-up)
2c	"Outcomes" Research; Ecological studies
3a	SR (with homogeneity*) of case-control studies
3b	Individual Case-Control Study
4	Case-series (and poor quality cohort and case-control studies§§)
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"

Oxford Centre for Evidence-based Medicine Levels of Evidence (May 2001)



Title	Journal	Method	Level	Outcome
Changes in treatment of advanced oropharyngeal cancer, 1985-2001.	Laryngoscope. 2007 Jan;117(1):16-21.	Case-series	4	No trial has been published that compared locoregional control and survival for patients treated with chemo-RT versus surgery.
Inoperable oropharyngeal carcinoma treated with concomitant irradiation, mitomycin C and bleomycin - long term results.	Neoplasma. 2005;52(2):165-74	prospective randomized clinical trial	1b	The loco-regional control, disease-free survival and overall survival at 5 years were 55% , 51% and 32% (95% CI: 44-67%, 41-62%, 22-42%), respectively
Concomitant radiochemotherapy with cisplatin (CDDP), 5-fluorouracil (5-FU) and mitomycin C (MMC) in locally advanced carcinoma of the oropharynx. Results of a phase II trial]	Bull Cancer. 1995 Dec;82(12):1044-51. Review. French	low quality RCT	2b	1. One and 2-year survival rates were 68 and 61% 2. severe digestive and haematological toxicity, which did not allow to conclude to the feasibility of this therapeutic association.
Current management of tonsillar cancer	Oral Oncol. 2003 Jun;39(4):337-42. Review		3a	advanced tonsil cancer represents a clinical challenge that requires multimodality therapy . advanced lesions are often treated with a combination of radiation, chemotherapy, and surgical ablation,.

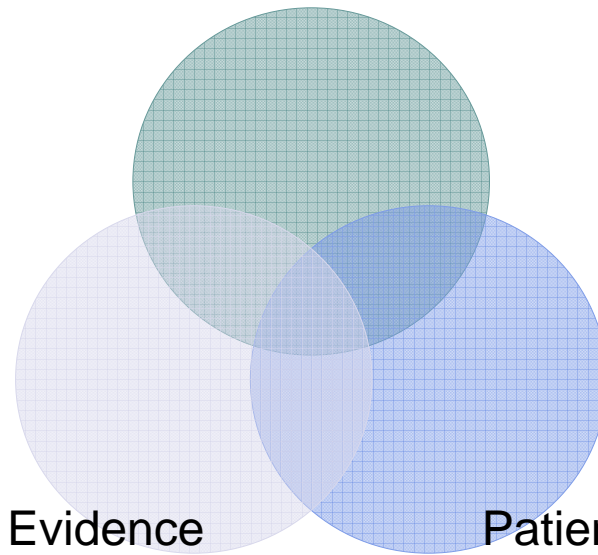


Advanced-staged tonsillar squamous carcinoma: organ preservation versus surgical management of the primary site	Head Neck. 2006 Jul;28(7):587-94.	case-control	3b	No significant difference in overall survival (OS) or freedom from relapse (FFR) by treatment was found
Organ preservation therapy using induction plus concurrent chemoradiation for advanced resectable oropharyngeal carcinoma: a University of Pennsylvania Phase II Trial.	J Clin Oncol. 2002 Oct 1;20(19):3964-71	Low-quality RCT	2b	<i>Actuarial survival</i> at 3 years was 70%, and <i>3-year event-free survival</i> was 59%. The 3-year <i>actuarial locoregional control</i> was 82%
Concurrent chemoradiation for locally advanced oropharyngeal cancer.	Am J Otolaryngol. 2007 Jan-Feb;28(1):3-8	case-series	4	the 3- and 5-year survival for the whole group were, respectively, 52% and 41%.
Treatment of advanced oropharyngeal cancers with chemotherapy and radiation	Ear Nose Throat J. 2003 May;82(5):367-70	case-series	4	Similar between surgery and CCRT

Apply



Clinical Expertise



Best Research Evidence

Patient Preference



- There is no sufficient evidence to determine which kind of treatment is better for this patient.
- We will consider both the patient's preference and doctor's expertise to give this patient a proper treatment.

**Thanks for your
attention.**

