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INVITED REVIEW

Laryngeal Carcinoma

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ABSTRACT

The management of laryngeal cancer is reviewed in the context of the Clinical Practice Guidelines of the Coordination Committee in Clinical Oncology of the Hospital Authority. The relative merits of surgery and radiotherapy for various tumour stages is discussed. Chemotherapy has not yet been shown to have a clear place in management, even for 'organ preservation'. Conventional fractionation of radiotherapy with 2 Gy/day for 5 days/week is no longer considered optimal; the Danish head and neck cancer regimen giving 6 fractions/week is suggested as an alternative standard.

Key Words: *Carcinoma, Chemotherapy, Larynx, Radiotherapy, Surgery*

The management of laryngeal carcinoma remains controversial as widely differing treatment policies are followed in various parts of the world. The only clinical situation where there is widespread agreement is for the management of the T4 primary with involvement of cartilage. Laryngectomy and postoperative radiotherapy is usually recommended because of low cure rates and poor laryngeal function, even if the tumour is controlled.

In early disease (T1-2 N0), a policy of radical radiotherapy has been popular for many years, reserving surgery for salvage of radiotherapy failures (RRSS). However, in many countries, especially southern Europe, radiotherapy is rarely used, having been supplanted by endoscopic laser resection and partial laryngectomy. There is a lack of controlled trials comparing the two protocols. Both result in some reduction in voice quality, with comparisons within the same centre tending to favour radiotherapy as giving a generally better voice.[1] The argument in favour of surgery is its relative simplicity and lower cost. Comparative data on survival and recurrence rates are lacking.

The treatment of T3 tumours, in which the vocal cord is fixed but there is no evidence of cartilage invasion or extra-laryngeal spread, has traditionally been by laryngectomy. Some centres, especially in Canada and northern Europe, have advocated a policy of RRSS for more than 40 years. Laryngologists in general have been unwilling to accept such a policy in the belief that many radiotherapy failures prove to be unresectable, with survival rates compromised in comparison to immediate laryngectomy. No randomised controlled trials comparing RRSS with laryngectomy have been completed.

The position has changed during the past 20 years with the introduction of neo-adjuvant chemotherapy. Squamous cell carcinomas of the head and neck, including the larynx, have shown a high response rate to cytotoxic drugs. In addition, a good response tended to be associated with a subsequent favourable outcome with radical radiotherapy.[2] This led to the introduction of so-called 'organ-sparing' protocols. Patients are given two courses of standard chemotherapy. If they are deemed to be good responders, they proceed to an RRSS policy, if not they undergo laryngectomy. This approach proved more acceptable to laryngologists who were averse to the idea of radical radiotherapy alone. Three randomised trials of this approach have been published to date. Meta-analysis of these studies by the Meta-Analysis of Chemotherapy on Head and Neck Cancer (MACH-NC) collaborative group revealed an absolute survival difference of 6% in favour of immediate laryngectomy over organ preservation, but this difference did not reach statistical significance.[3]

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There are several major criticisms levelled at organ preservation.[4] In head and neck cancer in general, neo-adjuvant chemotherapy has failed to have an impact on survival, as was also indicated in the MACH-NC meta-analyses.[3] Therefore, the only value of this chemotherapy is to serve as a predictive test of radiocurability, albeit not a particularly reliable one, as most laryngeal cancers respond. The trials need to be repeated with a RRSS arm without chemotherapy.

The Clinical Practice Guidelines of the Coordination Committee in Clinical Oncology of the Hospital Authority guidelines published in this issue succinctly summarise the surgical and radiotherapeutic alternatives for the various sites and stages of disease.[5] There is little with which most international experts in the field would disagree, except possibly the use of neo-adjuvant chemotherapy outside clinical trials. It is to be hoped that laryngologists and oncologists in Hong Kong will be able to formulate policies on the choice of treatment for the various sites and stages of laryngeal cancer, and perhaps conduct prospective trials to determine the best lines of management in their local context.

Fractionation for radiotherapy of laryngeal cancer has been a controversial subject for many years. Many schedules are in use, from the 16-fraction 3-week schedules devised at the Christie Hospital in Manchester,[6] to the 7- or 8- week schedules favoured by the pioneer Parisian radiotherapists. Five fractions/week of 2 Gy, to a total dose of 60-70 Gy became an international standard, and is recommended in the guidelines. However, many trials comparing other regimens with this standard as the control arm, have demonstrated superior results. Consequently, it is now becoming difficult to justify 2 Gy five times/week as routine therapy. For example, following the outcome of the British Institute of Radiology trial,[7] many UK radiotherapists now treat early laryngeal cancer with either 50 Gy in 16 fractions or 55 Gy in 20 fractions.

For more advanced tumours, several different altered fractionation schemes have proved superior to standard fractionation, and are mentioned in the guidelines. Of these the simplest and most economic is that used in the Danish head and neck cancer (DAHANCA) 6 and 7 studies,[8] namely an extra fraction on 1 day of the week, so that a total dose of 68 Gy is given in 34 fractions in just under 6 weeks. The DAHANCA results are among the world's best and, notably in supraglottic carcinoma, were achieved by the addition of the hypoxic-cell sensitiser, nimorazole.[9] Nimorazole is cheap and non-toxic, and should therefore be considered for wider use.

Chemotherapy concurrent with radiotherapy is mentioned in the guidelines as an option for advanced disease. Its use is supported by the MACH-NC meta-analysis, which showed a small but significant benefit — in contrast to neo-adjuvant chemotherapy. Not surprisingly, there is no recommendation for which drug(s) to use. A large number of different regimens have been tested, with no clear evidence of which is best. Cisplatin, with or without infusional fluorouracil, is certainly the most popular agent and could be advised as a standard.

All altered fractionation schemes and concomitant cytotoxic agents result in more severe acute radiation reactions, but these are usually acceptable and manageable. The limiting factor in radiotherapy is irreversible late normal tissue damage. This is not improved in any of the altered fractionation schemes mentioned. In the case of concurrent chemotherapy, however, there is a suggestion that cytotoxic drugs may enhance late damage,[10] so care is needed in the choice of both drug and radiation dosage.

In general the guidelines, although broad, provide a framework of accepted best practice for the treatment of laryngeal cancer. If all patients are treated according to these guidelines, survival rates would be expected to be in line with those from major cancer centres. Perhaps in future it will be possible for the guidelines to be made 'tighter', as outcome data from their use and evidence from clinical trials becomes available around the world.

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