Role of Radiotherapy in the Treatment of Nasoethmoidal Adenocarcinoma

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Objective: To assess the efficacy of radiotherapy in the treatment of nasoethmoidal adenocarcinoma.

Design: Multicenter, retrospective study.

Setting: Eleven French hospitals.

Patients: The medical records of 418 patients who presented with nasoethmoidal adenocarcinoma from January 1, 1976, through December 31, 2001, were evaluated. A total of 324 patients were treated with a combination of surgery and radiotherapy, and 55 were treated with surgery only.

Main Outcome Measures: Survival rates, disease recurrence, and postoperative complications.

Results: The 5-year Kaplan-Meier survey revealed survival rates of 64.5% for the surgery-only group and 70.8% for the combined-treatment group. In the surgery-only group, 28 patients (51%) had disease recurrence (24 local, 2 regional, and 2 distant). Of the 55 patients in the combined-treatment group, 31 patients (56%) had disease recurrence (29 local, 1 regional, and 1 distant). Immediate postoperative complications in the combined-treatment group were hemorrhages in 2 patients, meningitis in 3 patients, and cerebrospinal fluid leakage in 4 patients, but no deaths occurred. In the surgery-only group, 1 patient had meningitis, 2 had cerebrospinal fluid leaking but no hemorrhage, and 5 died postoperatively.

Conclusion: The results of this retrospective study suggest that radiotherapy can be used to treat nasoethmoidal adenocarcinoma, but its usefulness should be confirmed with further prospective studies.


Nasoethmoidal adenocarcinomas are rare tumors, yet the risk factors for these tumors have been previously well defined. The criterion standard treatment reported in the literature is the combination of surgery and radiotherapy, however, some authors have reported an alternative approach that does not include radiotherapy. The aims of this study were to evaluate and compare patients treated by surgery only with patients treated by a combination of methods (surgery and radiotherapy) and to assess the role of radiotherapy in this patient population.
The epidemiologic data of the 2 groups were similar, with nasoethmoidal adenocarcinoma occurring mostly in men in the sixth decade with a long period (>20 years) of wood particle exposure. The only difference in the data was that more women were in the surgery-only group, but sex was not a prognostic factor in this patient population. Unilateral rhinologic symptoms were routinely found. All patients underwent computed tomography, whereas magnetic resonance imaging was used for more recent patients included in the study. The risk factors of each group are reported in Table 1.

The 5-year Kaplan-Meier survey revealed survival rates of 64.5% for the surgery-only group and 70.8% for the combined-treatment group. No statistical difference was found in the survival rate (Kaplan-Meier) between these 2 groups (P = .20), but the rates were asymmetric, and more at-risk patients were present in the combined-treatment group. To eliminate this difference, a cross-matched population was created, and 55 patients treated by surgery and radiotherapy were selected to obtain 2 similar groups. Further analysis was performed to compare the surgery-only group to the cross-matched population of 55 patients treated with surgery and radiotherapy. The risk factors for prognosis were the size of the tumor (T4), the size of the lymph node, and intracranial involvement.1

Staging was performed according to the recommendations of the American Joint Committee on Cancer21 for the staging of tumors of the ethmoid sinuses. Both groups contained 7 patients with T1 tumors, 21 with T2 tumors, 11 with T3 tumors, and 16 with T4 tumors; all tumors were labelled N0 based on the American Joint Committee on Cancer classification. All centers included patients treated by surgery only. During this long period of analysis, combined treatment (surgery and radiotherapy) of these lesions experienced major advancements, but the distribution during this period in patients of the 2 groups subsequently permitted a more specific comparison.

Of the 55 patients in the surgery-only group, surgical resection was transfacial in 42 patients (76%), transcranial only in 3 patients (5%), combined (transfacial and transcranial) in 8 patients (15%), and endoscopic in 2 patients (4%). The 2 endoscopic procedures each revealed a poorly developed lesion in a unilateral polypl discovered fortuitously. The transfacial approach was preferred when the lesion was extensive to the mediofacial area with no dura or brain extension. The extension to the cribiform plate was not a contraindication to a transfacial approach for some surgeons. The transcranial procedure was specifically performed for the lesion with intracranial extension but with a limited extension to the anterior part of the sinonasal area.

Radiotherapy was external in all patients with no intensity-modulated radiotherapy or conformal radiation therapy. Megavoltage photons were used during a once-daily fractionation scheme with a median dose of 61 Gy (range, 50-70 Gy) in 30 fractions.

Statistical analysis was performed to evaluate the survival rate of the 2 populations. For statistical analysis we used log-rank and χ² tests, and data were analyzed using Statview statistical software, version 5.0 (SAS Institute Inc, Cary, North Carolina).

### RESULTS

The epidemiologic data of the 2 groups were similar, with nasoethmoidal adenocarcinoma occurring mostly in men in the sixth decade with a long period (>20 years) of wood particle exposure. The only difference in the data was that more women were in the surgery-only group, but sex was not a prognostic factor in this patient population. Unilateral rhinologic symptoms were routinely found. All patients underwent computed tomography, whereas magnetic resonance imaging was used for more recent patients included in the study. The risk factors of each group are reported in Table 1.

The 5-year Kaplan-Meier survey revealed survival rates of 64.5% for the surgery-only group and 70.8% for the combined-treatment group. No statistical difference was found in the survival rate (Kaplan-Meier) between these 2 groups (P = .20), but the rates were asymmetric, and more at-risk patients were present in the combined-treatment group. To eliminate this difference, a cross-matched population was created, and 55 patients treated by surgery and radiotherapy were selected to obtain 2 similar groups with regard to risk factors and general data (Table 2). The 5-year Kaplan-Meier survey revealed a survival rate of 60.9% for the cross-matched group. No statistical difference was found with regard to the survival rate between these 2 comparative groups for risk factors of worse prognosis (P = .60) (Figure). All patients included in this analysis underwent a surgical procedure. The macroscopic and microscopic analyses of the tumor resection are given in Table 3.

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### Table 1. Risk Factors of the Patients in the Surgery-Only and Combined-Treatment Groups

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Surgery Only (n=55)</th>
<th>Combined Treatment (n=324)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain or dura involvement</td>
<td>7 (2.7)</td>
<td>75 (23.1)</td>
</tr>
<tr>
<td>Stage T4 tumor</td>
<td>16 (29.1)</td>
<td>120 (37.0)</td>
</tr>
<tr>
<td>Lymph node involvement</td>
<td>0 (0)</td>
<td>7 (2.2)</td>
</tr>
</tbody>
</table>

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### Table 2. Characteristics of the Surgery-Only and Combined-Treatment Groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Surgery-Only Group (n=55)</th>
<th>Combined-Treatment Group (n=55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>6 (11)</td>
<td>6 (11)</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>63.27 (9.75)</td>
<td>63.10 (9.75)</td>
</tr>
<tr>
<td>Wood particle exposure</td>
<td>47 (85)</td>
<td>43 (78)</td>
</tr>
<tr>
<td>Leather exposure</td>
<td>1 (2)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Duration of exposure, mean (SD), y</td>
<td>25.45 (13.9)</td>
<td>25.71 (13.9)</td>
</tr>
<tr>
<td>Brain or dura involvement</td>
<td>7 (13)</td>
<td>7 (13)</td>
</tr>
<tr>
<td>Stage T4 tumor</td>
<td>16 (29)</td>
<td>16 (29)</td>
</tr>
<tr>
<td>Lymph node involvement</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

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*a* Data are presented as number (percentage) of patients unless otherwise indicated.

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In the surgery-only group, 28 patients (51%) had disease recurrence (24 local, 2 regional, and 2 distant). Of the 55 patients in the combined-treatment group, 31 (56%) had disease recurrence (29 local, 1 regional, and 1 distant). At the end point of this study, 32 patients in the surgery-only group and 31 in the combined-treatment group were disease free.

Immediate postoperative complications in the combined-treatment group were hemorrhages in 2 patients, meningitis in 3 patients, and cerebrospinal fluid leaking in 4 patients, but no deaths occurred. In the surgery-only group, 1 patient had meningitis, 2 had cerebrospinal fluid leaking but no hemorrhage, and 5 died postoperatively. Five patients had a T4 lesion and underwent a transcranial procedure.

<table>
<thead>
<tr>
<th>Tumor Margin</th>
<th>Surgery-Only Group (n=55)</th>
<th>Combined-Treatment Group (n=55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macroscopic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limit</td>
<td>12 (22)</td>
<td>8 (15)</td>
</tr>
<tr>
<td>Large</td>
<td>43 (78)</td>
<td>47 (85)</td>
</tr>
<tr>
<td>Microscopic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sufficient</td>
<td>39 (71)</td>
<td>40 (73)</td>
</tr>
<tr>
<td>Marginal</td>
<td>4 (7)</td>
<td>9 (16)</td>
</tr>
<tr>
<td>Insufficient</td>
<td>12 (22)</td>
<td>6 (11)</td>
</tr>
</tbody>
</table>

COMMENT

Although nasoethmoidal adenocarcinoma is rare, it is a well-defined condition. Epidemiologic, clinical, and radiologic findings have been reported in a number of articles. Risk factors are now well known, and the most important appear to be the size of the lesion (T4 in TNM classification), extension to the lymph node, and intracranial involvement. With regard to treatment, the criterion standard seems to be combined treatment (ie, combination of surgery and radiotherapy in most reported studies), which has a 5-year patient survival rate of 35% to 70%. The use of combination treatment is supported by the risk of local tumor recurrence. However, the effect of radiotherapy remains unclear. For some authors, adenocarcinoma of the sinuses and nasal cavities seems to be moderately radiosensitive, whereas other authors report radiotherapy as their treatment of choice. Some authors reserved radiotherapy for lesions with a large extension. More focused radiation, such as intensity-modulated radiotherapy, must be evaluated. In some cases, authors reported their experiences. Unfortunately, in those studies, data with regard to different histologic types of nasosinus tumors (such as epidermoid and esthesioneuroblastoma) were pooled. Hence, it was not possible to ascertain which data referred merely to adenocarcinoma of the ethmoid. In 2 recent reports, the 5-year overall survival rates were 45% and 58%, with no significant improvements in disease control but a low incidence of complications. The effect of surgery only was studied by Sisson et al but only in 2 patients with nasoethmoidal adenocarcinoma, who had a 5-year survival rate of 86%. For Sisson et al, surgery only was a valid alternative for the treatment of small and selected lesions. In the meta-analysis by Dulguerov et al, the comparison between surgery only (70%) and a combination of surgery and radiotherapy (63%) showed no statistical difference, but different types of lesions and various anatomical sites were added in their 2 groups.

In our series, of exclusive adenocarcinoma of the ethmoid bone, we found a 5-year survival rate of 69%, in accordance with the literature. The 5-year survival rate of the group treated by surgery only was 65.4%. In contrast to cases reported in the literature, no statistical difference was found with regard to a 5-year survival rate of the global population compared with the group treated by combined methods or the cross-matched group. Different hypotheses, depending on the size of the lesion, may explain this result.

With or without postsurgical radiotherapy, the aggressive lesions (T4 or those that involve lymph nodes, brain, or dura) had a poor prognosis, and the quality of life of these patients who forego aggressive treatment must be preserved. For smaller lesions, the use of surgery only may be sufficient to eliminate these small tumors, or postsurgical radiotherapy can be performed to effectively treat the curable lesion. This retrospective study was not able to determine the definitive therapeutic treatment, but our results indicate there is no advantage to the use of radiotherapy. Future major multicenter studies are needed to more precisely define the role of radiotherapy in treating nasoethmoidal adenocarcinoma.

In conclusion, the criterion standard treatment of ethmoid nasal adenocarcinoma is a combination of surgery and postoperative radiotherapy. This study demonstrates that all patients do not require postsurgical radiotherapy and selected patients can be treated by surgery only. Prospective studies will be useful to clarify the role of radiotherapy and develop a subsequent therapeutic strategy. New modalities of radiotherapy (eg, intensity-modulated radiotherapy) can perhaps improve the treatment of this condition. New molecules (eg, monoclonal antibody of epidermal growth factor receptor inhibitor) could be of interest in the treatment of these lesions, which are similar to intestinal adenocarcinomas. To our knowledge, no previous studies have examined the role of chemotherapy in the treatment of this condition. The results of this retrospective study suggest that radiotherapy can be used to treat nasoethmoidal adenocarcinoma, but its usefulness should be confirmed with further prospective studies.

Submitted for Publication: December 4, 2008; final revision received June 26, 2009; accepted June 29, 2009. Correspondence: Olivier Choussy, MD, ENT Department, Rouen University Hospital, 1 rue de Germont, 76031 Rouen, CEDEX France (olivier.choussy@chu-rouen.fr).

Author Contributions: Dr Choussy had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Studying the design: De Raucourt and Dehesdin. Acquisition of data: Ferron, Védrine, Toussaint, Liétin, Marandas, Babin, Rey, Cosmidis, and Makeiief. Analysis and interpretation of data: Choussy. Drafting of the manuscript: Choussy. Critical revision of the manuscript for important intellectual content: Ferron, Védrine, Toussaint, Liétin, Marandas, Babin, De Raucourt, Rey, Cosmidis, Makeiief, and Dehesdin. Obtained funding: Cosmidis. Administrative, technical, and material support: Choussy, Ferron, Toussaint, Marandas, De Raucourt, Rey, and Makeiief. Study supervision: Védrine, Babin, De Raucourt, and Dehesdin.

Financial Disclosure: None reported.

Additional Contributions: Richard Medeiros, PhD, Medical Editor at Rouen University Hospital, edited the manuscript and Jean François Menard, MD, PhD, Rouen University Hospital, provided expert advice in statistical analysis.

REFERENCES


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