Résumé


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Mots clés : Cancer thyroïdien ; Incidence ; Survie ; Mortalité ; Type histologique
Abstract

Objectives. – Describe time trends of incidence and mortality associated with thyroid cancer and provide 1 and 5-year survivals by histological group in French areas covered by cancer registries. Material and methods. – Data for 1975 to 2004 were provided by one thyroid-dedicated and 11 general registries. Incidence estimates were obtained by correction of incidence from areas with registries, then projections for 2008 were derived. Overall and relative survivals by sex and age (diagnosis period 1989–1997; cut-off date 1st January 2002) were obtained from the dedicated and nine other registries. Comparisons between areas or time periods used world-standardized rates. Results. – Between 1980 and 2005, incidence increased but mortality decreased in men and women. Annual cases increased five times and projections for 2008 were 8,000 cases and 400 deaths. The main increasing subtype was papillary carcinoma. One-year overall and relative survivals were 92 and 94%, respectively. Five-year overall and relative survivals were 87 and 93%, respectively. The highest survival (> 94%) concerned papillary carcinomas and the lowest (< 15%) anaplastic carcinomas. Survivals were generally higher in women than in men; precisely, higher in women for papillary and follicular carcinomas but higher in men for medullary and anaplastic carcinomas. Survivals increased with age, but for medullary carcinomas. Survivals from anaplastic carcinomas were very low whatever the age. Conclusion. – The increase of thyroid cancer frequency is dramatic but survivals are improving. Though the prognosis of the most increasing histological subtype is generally good, it remains very important to identify the causes of this steady increase to implement adequate preventive measures.

Keywords: Thyroid cancer; Incidence; Survival; Mortality; Histological type

1. Introduction

Until recently, in France, the incidence and mortality associated with thyroid cancer were not very high. However, although the number of deaths from thyroid cancer remains low (less than 1% of all cancer deaths in both sexes), the incidence of thyroid cancer in women is now the 5th leading cancer site; in 2005, it accounted for 3.7% of all cancers in women, whereas, in 1980, it accounted for only 1.4% of all newly diagnosed cancers and was ranking the 13th [1].

These facts reflect major changes in the frequency of this cancer over the last 20 years. In the present article, we describe the main features of:

- the incidence of and mortality due to all subtypes of thyroid cancer in France;
- the incidence by subtypes in French départements covered by cancer registries. We also report survival estimates relative to the various morphologies of this cancer.

2. Material

The data used for the above estimates correspond to the period 1975 to 2004 and were supplied by one registry dedicated to thyroid cancers (Marne-Ardennes) and 11 other general registries (Doubs, Calvados, Isère, Bas-Rhin, Somme, Tarn, Haut-Rhin, Hérault, Manche, Loire-Atlantique, and Vendée) [1].

The detailed data, with classification by subtypes, were obtained from the seven oldest registries (Marne-Ardennes, Calvados, Doubs, Isère, Bas-Rhin, Somme, and Tarn). National incidence estimates per thyroid cancer subtypes cannot be obtained because National mortality data do not always mention these subtypes. Thus, the distribution of thyroid cancers according to subtypes had to be based on the more detailed cancer registry records.

Survivals of patients aged 15 and over were obtained from the thyroid-specialized and nine other general registries (Loire Atlantique and Vendée were excluded because their data collection was only recently started). The period of diagnosis was 1989 to 1997 and the cut-off date was set at the 1st January 2002 with active search for vital status. The overall percentage of “lost to follow-ups” was 6.9% and ranged from 3.4% (for anaplastic thyroid cancer) to 8.2% (for follicular thyroid cancer).

3. Methods

In the absence of a nationwide cancer registry, French national incidence estimates were obtained by applying a correction factor to incidence data from areas with registries. This correction factor was the ratio of the mortality over the whole country to the mortality in all registry areas. This method was detailed in an article by Belot et al. [1] and used to obtain national estimates for the period 1980 to 2005.

The above-cited estimation method made it possible to derive incidence projections for 2008 [2]. These projections are subject to a high degree of uncertainty because they are based on the assumption that past trends will continue.

To compare results between geographical areas or different time periods differing by population age structures, the rates were world-standardized.

Survival analyses were carried out in terms of overall survival (death whatever its cause) and relative survival; the latter indicator enabled estimating cancer-specific survival, i.e. survival that would be observed if thyroid cancer were the only cause of patient death. This estimation was made using an approach described elsewhere [3–5]. Survival was estimated by sex, age, and period of diagnosis on all thyroid cancer subtypes confounded but by sex and age only per each subtype.

4. Results


National French estimates of thyroid cancer showed constant and regular increases in incidence (Table 1 and Fig. 1) but
Table 1
Thyroid cancer incidence and mortality rates in France (1980–2008; World-standardized per 100,000).
Données d’incidence et de mortalité par cancer de la thyroïde en France (1980–2008 ; standardisées monde pour 100 000 personnes).

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<td><strong>Incidence</strong></td>
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</tr>
<tr>
<td>Men</td>
<td>1.0</td>
<td>1.3</td>
<td>1.7</td>
<td>2.3</td>
<td>3.1</td>
<td>4.2</td>
<td>5.0</td>
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<tr>
<td>Women</td>
<td>2.9</td>
<td>3.9</td>
<td>5.2</td>
<td>7.0</td>
<td>9.5</td>
<td>12.7</td>
<td>15.2</td>
</tr>
<tr>
<td><strong>Mortality</strong></td>
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<tr>
<td>Men</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.3</td>
<td>0.3</td>
<td>0.2</td>
<td>−1.8</td>
</tr>
<tr>
<td>Women</td>
<td>0.6</td>
<td>0.6</td>
<td>0.5</td>
<td>0.4</td>
<td>0.4</td>
<td>0.3</td>
<td>−3.1</td>
</tr>
</tbody>
</table>

For 2008, data correspond to projections based on the assumption that the trend observed over the period 1980 to 2004 will continue until 2008.

Also constant and regular decreases in mortality rates in men and women. The annual trends over the 2000 to 2005 period showed that the increase in incidence and the drop in mortality were especially marked by the end of that period (Table 1). Throughout the period, the incidence was three times higher in women than in men.

Between 1980 and 2005, there was a five-fold increase in the annual number of cases diagnosed in both sexes (Table 2). The largest part of that rise (82%) corresponded to an increased risk and the remaining part (18%) to demographic changes: population increase between 1980 and 2005 (14%) and progressive ageing in both sexes (4%).

According to projections for 2008 made on the basis of trends observed between 1980 and 2004, the number of new cases of thyroid cancer should exceed 8,000 and the number of deaths be about 400.

Table 2
Number of thyroid cancer cases and deaths estimated in France (1980–2008).

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<td><strong>Incidence</strong></td>
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</tr>
<tr>
<td>Men</td>
<td>325</td>
<td>421</td>
<td>571</td>
<td>794</td>
<td>1119</td>
<td>1599</td>
<td>1980</td>
</tr>
<tr>
<td>Women</td>
<td>1027</td>
<td>1352</td>
<td>1844</td>
<td>2572</td>
<td>3607</td>
<td>5073</td>
<td>6214</td>
</tr>
<tr>
<td><strong>Mortality</strong></td>
<td></td>
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<tr>
<td>Men</td>
<td>151</td>
<td>153</td>
<td>152</td>
<td>151</td>
<td>150</td>
<td>147</td>
<td>140</td>
</tr>
<tr>
<td>Women</td>
<td>345</td>
<td>339</td>
<td>324</td>
<td>302</td>
<td>280</td>
<td>256</td>
<td>244</td>
</tr>
</tbody>
</table>

For 2008, data correspond to projections based on the assumption that the trend observed over the period 1980 to 2004 will continue until 2008.
Table 3
Distribution of new thyroid cancer cases by subtype, time period, and sex.
Distribution des nouveaux cas de cancer de la thyroïde par sous-type, période et sexe.

<table>
<thead>
<tr>
<th></th>
<th>Papillary</th>
<th>Follicular</th>
<th>Medullary</th>
<th>Anaplastic</th>
<th>Other</th>
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<tbody>
<tr>
<td></td>
<td>Cases (%)</td>
<td>Incidence rate</td>
<td>Cases (%)</td>
<td>Incidence rate</td>
<td>Cases (%)</td>
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</tr>
<tr>
<td>Men</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>1980–84</td>
<td>62 (43.7)</td>
<td>0.53</td>
<td>33 (23.2)</td>
<td>0.26</td>
<td>14 (9.9)</td>
</tr>
<tr>
<td>1985–89</td>
<td>101 (54.9)</td>
<td>0.74</td>
<td>41 (22.3)</td>
<td>0.28</td>
<td>21 (11.4)</td>
</tr>
<tr>
<td>1990–94</td>
<td>157 (60.9)</td>
<td>1.11</td>
<td>60 (23.3)</td>
<td>0.42</td>
<td>24 (9.3)</td>
</tr>
<tr>
<td>1995–99</td>
<td>251 (70.3)</td>
<td>1.67</td>
<td>49 (13.7)</td>
<td>0.30</td>
<td>34 (9.5)</td>
</tr>
<tr>
<td>2000–04</td>
<td>439 (72.9)</td>
<td>2.77</td>
<td>83 (13.8)</td>
<td>0.50</td>
<td>50 (8.3)</td>
</tr>
<tr>
<td>Total</td>
<td>1010 (65.5)</td>
<td></td>
<td>266 (17.2)</td>
<td></td>
<td>143 (9.3)</td>
</tr>
<tr>
<td>Women</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>1980–84</td>
<td>214 (47.4)</td>
<td>1.76</td>
<td>124 (27.4)</td>
<td>0.96</td>
<td>15 (3.3)</td>
</tr>
<tr>
<td>1985–89</td>
<td>391 (62.3)</td>
<td>2.88</td>
<td>151 (24.0)</td>
<td>1.02</td>
<td>31 (4.9)</td>
</tr>
<tr>
<td>1990–94</td>
<td>666 (72.4)</td>
<td>4.57</td>
<td>164 (17.8)</td>
<td>1.03</td>
<td>37 (4.0)</td>
</tr>
<tr>
<td>1995–99</td>
<td>1093 (78.8)</td>
<td>7.19</td>
<td>177 (12.8)</td>
<td>1.07</td>
<td>54 (3.9)</td>
</tr>
<tr>
<td>2000–04</td>
<td>1630 (83.9)</td>
<td>10.01</td>
<td>202 (10.4)</td>
<td>1.18</td>
<td>52 (2.7)</td>
</tr>
<tr>
<td>Total</td>
<td>3994 (74.9)</td>
<td></td>
<td>818 (15.4)</td>
<td></td>
<td>189 (3.6)</td>
</tr>
</tbody>
</table>

a Tarn and Somme registries had no data for the years 1980 and 1981.
b World-standardized per 100,000.

4.2. French registry data on the incidence of thyroid cancer by histological subtype

Data in Table 3 show that the main increase in thyroid cancer incidence concerned the papillary subtype whereas the incidence of other subtypes (follicular and medullary) increased only slightly and that of the anaplastic subtype even decreased. Over 20 years, the incidence of papillary thyroid cancer was multiplied by 5.2 in men and 5.7 in women and the world-standardized rates increased from 0.53 to 2.77 in men and from 1.76 to 10.0 in women.

Between 1985 and 1989, the percentages of the papillary subtype relative to all thyroid cancers were 55% in men and 62% in women. From 2000 to 2004, these percentages increased up to 73% in men and 84% in women. The previous period (1980–1984) provided poor information because of a high percentage of "subtype: unspecified".

The distribution of thyroid cancers by subtypes was highly dependent on the age at diagnosis (Table 4). Although papillary carcinoma was the most frequent in all age groups, its proportion decreased sharply in people over 75 years of whom almost a quarter had anaplastic carcinomas.

In the recent period (2000–2004), the incidence of papillary thyroid cancer varied widely between départements (Fig. 2) whereas the incidence of other subtypes (non-papillary) was more homogeneous. Thus, incidence differences between the eight départements can be attributed to differences in observed papillary carcinomas in both sexes.

4.3. French registry data on survival from thyroid cancer

In general, the prognosis of thyroid cancer was very good (Table 5). At 1-year, the overall survival was 92% and the relative survival 94%. At 5-years, these survival rates were 87% and 93%, respectively. However, the estimates included two extremely contrasting situations: very high survival rates for papillary carcinoma (5-year overall and relative survivals of 94% and 99%, respectively) and very low survival rates for anaplastic carcinoma (5-year overall and relative survivals of 10% and 15%, respectively).
Considering all histological subtypes combined, survival was higher in women than in men. However, whereas survival was higher in women as regards papillary and follicular carcinomas, it was higher in men as regards medullary and anaplastic carcinomas. In women with anaplastic carcinoma, the 5-year overall and relative survivals were extremely low (6% and 9%, respectively). However, because the number of anaplastic carcinomas was low (93, of whom 64 women), the confidence intervals of the survival estimates were very wide.

Generally, survival decreased with age but for medullary carcinoma; however, the latter subtype was rare. This decrease, expected for overall survival, was also found for relative survival. Survival decreased markedly after age 75 years. Considering all subtypes, the 5-year relative survival ranged from 98% in the 15 to 44 years old category to 51% in category 75 years and over. This decrease was less marked for papillary carcinoma; the 5-year relative survival ranged from 100% in the 15 to 44 years old category to 80% in category 75 years and over. Concerning anaplastic carcinomas, survival was very low at all ages.

Survival from thyroid cancer, all subtypes confounded, is improving over time; the 5-year relative survival increased from 89% for the cases diagnosed between 1989 and 1991 to 96% for the cases diagnosed between 1995 and 1997. That increase was also true for one-year survival.

5. Discussion

In France, as in most Western countries, the incidence of thyroid cancer has been dramatically increasing over the last 20 years or more [6–7]. In 2005, thyroid cancer became the 5th ranking cancer site in France in terms of incidence in women [1].

This increase concerned almost exclusively papillary carcinomas and is most probably linked to technical and diagnostic progresses [8–9]. A previous description of trends in the incidence of papillary carcinomas by tumor size based on data from six French cancer registries has implicitly confirmed this increase by showing a very marked increase in micropapillary carcinomas, particularly in those less than 5 mm diameter [10].

Improvements in diagnosis may have also been responsible for the increase in the incidence of follicular carcinomas. Thus, the near-stability in the rate of follicular carcinomas may seem surprising but can be explained by changes in the anatomopathological definitions. Actually, in 1975, the WHO guidelines stipulated that any follicular carcinoma with a papillary component should be classified as papillary. Also, in 1988, nuclear criteria for papillary carcinomas were introduced resulting in tumors with a purely follicular architecture being classified as papillary. These guidelines were gradually adopted in France by all anatomopathologists and used by registries in the late 1980s and early 1990s. Thus, a large proportion of carcinomas previously classified as follicular or mixed are now classified as papillary.

Another factor that may specifically explain the decrease in follicular carcinomas is the disappearance of iodine deficiency.

Among the hypotheses put forward to explain the increased incidence of thyroid cancer is the impact of the radioactive fallout from the Chernobyl nuclear accident. Although this hypothesis cannot be completely discarded, especially that results of several French case-control studies are awaited, it does not seem very plausible given the regular increases both in time (already before 1986) and in place (in areas less affected by the fallout, such as the Tarn Département in Southwestern France). A recent publication by Cardis et al. [12] has shown that, except in heavily contaminated areas, it is not easy or possible to show correlations between increased incidence and radioactive fallouts.

The scientific literature mentioned several other risk factors, essentially occupational and environmental. On this subject, one may refer to a recent review by Leux et Guénel [13] who underscored the genotoxicity of a number chemical products. The heterogeneity of cancer incidence in different French départements is mirrored worldwide. In the latest report on Cancer incidence in five continents that incorporated data from 300 registries and covered the period 1998 to 2002 [14], the registry of département Tarn, near the Spanish border, reported the 5th highest incidence, whereas that of département Bas-Rhin, on the German border, reported the 194th.

In the present study, survival from papillary or follicular carcinomas was higher in women than in men but survival from medullary and anaplastic carcinomas was higher in men than...
in women. Let us note however that the estimates relative to the latter two subtypes were not very accurate. Because most of these differences are not very marked, they are seldom mentioned in the scientific literature. Akslen et al. [15] did not find sex-specific differences concerning survival. Cunningham et al. [16] and Colonna et al. [17] have already mentioned a higher survival in women as regards papillary and follicular carcinomas. Guilliland et al. [18] observed similar survivals in men and women as to papillary and follicular carcinomas, poorer survivals in women than in men as to anaplastic carcinomas, and higher survivals in women than in men as to medullary carcinomas. Finally, contrarily to our observations on medullary carcinomas, Esik et al. [19] observed higher survivals in women than in men.
Age-related differences were much greater than sex-related ones. Moreover, the literature has confirmed that age is an important prognostic factor [15–19]; indeed, it was the only prognostic factor we kept in our analyses. However, another very influential prognostic factor, the cancer stage at the time of diagnosis, should have been considered as well but that information was not available for all analyzed cases. The effect of cancer stage at diagnosis is certainly associated with the very high survivals of patients with papillary carcinoma and the survival increase over the period 1987 to 1994 [5], during which small tumors were predominant [10].

6. Conclusion

The ever increasing frequency of thyroid cancer is becoming a real public health problem in women, even though the specific survival is extremely high. Thus, as some authors [20] seem to note a slow-down of that frequency in the French Rhône-Alpes Region (eight départements) whereas others report completely different results elsewhere, such as in the United States [21], it remains of utmost importance to closely monitor the disease trends and make better estimates of required resources.

7. Conflicts of interest

The authors have not declared any conflict of interest.

8. French version

A french version of this article is available at doi:10.1016/j.ando.2009.11.003.

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References