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# The Causes of Formation and the Surgical Treatment of Recurrent Goiter

# Przyczyny powstawania oraz leczenie chirurgiczne wola nawrotowego

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#### **Abstract**

**Background.** Recurrent goiter is the regrowth of thyroid tissue after strumectomy. Its causes include the strategy of surgical treatment and the kind of substitution therapy after operation.

**Objectives.** The aim of this study was to analyze the causes of recurrent goiter formation.

**Material and Methods.** Fifty-six patients with recurrent goiter were operated on in 1991–2000. In accordance with the procedures and terminology of the Bayes methods for data analysis, three types of statistical model were used: the binomial-beta hierarchical model, the Cox proportional hazard model, and the Weibull regression model. Significant results are reported.

**Results.** In the patients who received substitution therapy after the primary operation, the percentage of recurrences was one sixth of that of the group who received no substitution therapy. Recurrence was faster in patients who were older at the time of the primary operation. The risk of recurrence increased with time after the primary operation. The percentage of true recurrent goiter in this material was 73% and pseudo-recurrent 27%. Pseudo-recurrence was mostly in a non-operated lobe (67%), rarely in the pyramidal lobe (20%) and isthmus (13%). The mean time of true recurrence was 19 and of pseudo-recurrence 11 years.

**Conclusions.** Because of the high percentage of pseudo-recurrences after strumectomy and the short time of their formation, the primary operation should be based on pyramidal lobe removal and be bilateral and sufficiently complete, with excision of both lobes. Postoperative substitution therapy reduces the rate of goiter recurrence. The primary operation for goiter should be performed promptly after its diagnosis because recurrence is faster in older people. After the primary operation the patients should be monitored for several years to diagnose recurrence as early as possible (**Adv Clin Exp Med 2009, 18, 6, 595–599**).

**Key words:** recurrent goiter, strumectomy.

#### Streszczenie

**Wprowadzenie.** Wole nawrotowe jest odrostem tkanki tarczycowej powstającym po operacji wycięcia wola. Za przyczynę nawrotu uznaje się między innymi strategię postępowania chirurgicznego oraz rodzaj terapii substytucyjnej po zabiegu usunięcia tarczycy.

Cel pracy. Analiza przyczyn odrostów wola u chorych operowanych wtórnie.

**Materiał i metody.** Do badań włączono 56 chorych z nawrotem wola, którzy byli leczeni operacyjnie w latach 1991–2000. W pracy zgodnie z procedurami obliczeniowymi i terminologią założeń pełnego modelowania bayesowskiego zostały zaadoptowane następujące typy kompleksowych modeli statystycznych: hierarchiczny model beta-dwumianowy, model proporcjonalnego ryzyka Coxa, model regresji Weibulla. Po dokonaniu obliczeń statystycznych podano wartości oczekiwane będące wynikami istotnymi.

Wyniki. W grupie chorych, u których zastosowano substytucję po operacji pierwotnej odsetek nawrotów był 6-krotnie mniejszy niż w grupie, gdzie nie stosowano pooperacyjnej profilaktyki hormonalnej. U chorych w starszym wieku, operowanych pierwotnie, szybciej dochodzi do powstania nawrotu wola. Ryzyko powstania nawrotu zwiększa się w miarę upływu czasu po pierwotnej strumektomii. Odsetek stwierdzonych w materiale nawrotów prawdziwych wola wyniósł 73%, a rzekomych 27%. Nawrót rzekomy wola najczęściej dotyczył płata nieoperowanego (67%), znacznie rzadziej płata piramidowego (20%) oraz cieśni (13%). Średni czas powstawania nawrotu prawdziwego wyniósł 19 lat, a nawrotu rzekomego 11 lat.

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Wnioski. W związku ze znaczącym odsetkiem nawrotów rzekomych po operacjach wola i krótkim czasem ich powstawania operacja pierwotna powinna polegać na usunięciu płata piramidowego oraz obustronnym, dostatecznie doszczętnym, wycięciu obu płatów w granicach zdrowych tkanek. Stosowanie substytucji w pooperacyjnej profilaktyce hormonalnej zmniejsza odsetek nawrotów wola. Podczas zdiagnozowania wola należy odpowiednio szybko przeprowadzić zabieg operacyjny, gdyż u osób starszych szybciej dochodzi do nawrotu choroby. Pacjenci po zabiegu operacyjnym przez kilkanaście lat powinni pozostawać pod kontrolą lekarską, aby jak najszybciej uchwycić nawrót choroby (Adv Clin Exp Med 2009, 18, 6, 595–599).

Słowa kluczowe: wole nawrotowe, strumektomia.

The mechanisms of recurrent goiter formation are not completely explained [1-3]. The most probable causes are the same which lead to the formation of endemic or sporadic goiter. These are iodine deficiency and genetic, autoimmunological, and enzymatic factors. Elevated thyroid-stimulating hormone (TSH) level, increased number of TSH receptors, and defects in thyroid hormone synthesis are also mentioned. A well-performed primary operation can successfully prevent recurrence. One of the causes of recurrent goiter formation is the insufficient extent of strumectomy (excision of a goiter) during the first operation [1, 7–11]. Excision of only one lobe or solitary adenoma and leaving the second lobe intact can lead to pseudorecurrence (recurrence in the previously non-operated lobe), which should be distinguished from true recurrence, which occurs after excision of two lobes with the isthmus and pyramidal lobe [4, 6, 10, 12–14]. The other very important factor which is stressed by many authors as a cause of recurrence is a lack of substitution therapy after the first operation. Postoperative prophylaxis with L-thyroxine (levothyroxine) can effectively prevent recurrence and reduce the size of recurrent goiter [1, 2, 4, 10, 11, 14–21]. There is also a group of authors who are against substitution therapy because they do not find a connection between it and the recurrence of goiter [22–26].

### **Material and Methods**

Fifty-six patients who had primary operations in 1945–1955 were investigated. They were operated on for recurrent goiter in the County Hospital in Opole in 1991–2000. In this group were 54 (96.4%) women and 2 (3.6%) men (Fig. 1). The youngest patient was 19 and the oldest 71 years old. The mean age was 53 years. The mean age of the women with recurrent goiter was 53.5 and of the men 50.5 years. The primary operation was performed in twenty patients in another hospital. The postoperative efficacy of substitution therapy after the primary operation was evaluated.

According to the procedures and terminology of Bayes' methods of data analysis, three types of statistical model were used. The binomial-beta hierarchical model was used to determine the probability of goiter recurrence in relation to risk factors and study group [27]. The Cox proportional hazard model was used to determine the hazard curves of disease incidence in relation to patient age [28]. The Weibull regression model was used to determine the mean age of disease incidence [29]. Significant results are reported here.

# **Results**

The largest groups of patients were aged 41-50 (mean: 19) and 61-70 (mean: 17) years. The interval between the primary and secondary operation was between 1 and 47 years. The mean time of recurrence was 17 years. The recurrence of goiter mostly occurred 11-20 years after the primary operation. According to the statistical analysis, the risk of recurrence increased with time after the primary operation. Ten years after the primary operation the risk of recurrence was 30%, after 20 years 60%, and after 40 years 90% (Fig. 2). Recurrence was slower in patients who had the primary operation when younger. The percentage of real recurrent goiter was 73% and of pseudorecurrent 27% (Fig. 3). Pseudo-recurrence occurred mostly in a non-operated lobe (67%), rarely in pyramidal lobe (20%) and isthmus (13%) (Fig. 4). Pseudo-recurrence was four times more frequent than real recurrence in the first 5 years and was also more frequent 6-10 years after the primary operation (Fig. 5). The mean time of real recurrence was 19 years and of pseudo-recurrence was 11 years (Fig. 6).

The patients who had their primary operation at the County Hospital in Opole were divided into three subgroups according to their substitution therapy after the primary operation: those operated on in 1958–1970 (no substitution), those operated on in 1971–1985 (Thyroideum, Polfa), and those operated on in 1986–2000 (L-thyroxine). According to the statistical analysis, the percentage of recurrence in the subgroup treated with L-thyroxine was four times lower than in the subgroup treated with Thyroideum and six times lower than in the subgroup in which no substitution was used (Fig. 7).

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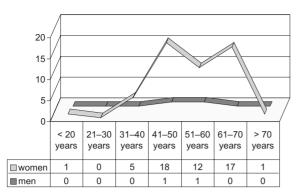
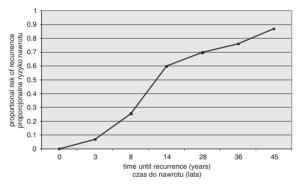


Fig. 1. The ages of the women and men operated on for recurrent goiter

**Ryc. 1.** Wiek kobiet i mężczyzn operowanych z powodu nawrotu wola



**Fig. 2.** The proportional risk of goiter recurrence with time (Cox model)

**Ryc. 2.** Proporcjonalne ryzyko nawrotu wola w czasie (model Coxa)

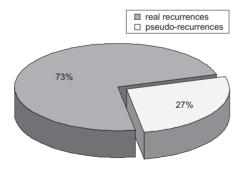
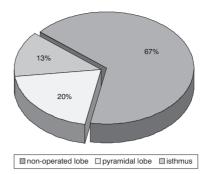


Fig. 3. Percentages of real and pseudo-recurrences

Ryc. 3. Odsetek nawrotów prawdziwych i rzekomych

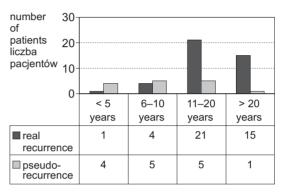
## **Discussion**

In the country's leading centers which specialize in goiter surgery, the percentage of recurrence does not exceed 1%. Barczyński found 0.6% recurrence in his material and Stajgis 0.8% [2,4]. Because of the high percentage of pseudo-recurrences and the short time of their formation, the primary operation should be based on pyramidal



**Fig. 4.** The distribution of recurrences in pseudo-recurrent goiter

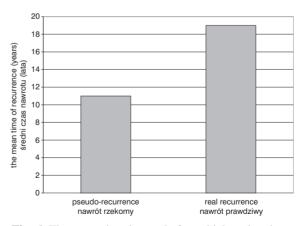
**Ryc. 4.** Umiejscowienie zmian w nawrotach rzekomych wola



time until recurrence czas do nawrotu

Fig. 5. Time intervals after which real and pseudorecurrence occurred

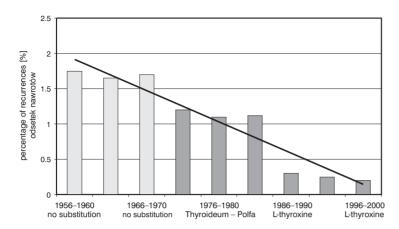
**Ryc. 5.** Odstępy czasu, po których następował nawrót wola prawdziwy i rzekomy



**Fig. 6.** The mean time interval after which real and pseudo-recurrence occurred (Weibull regression)

**Ryc. 6.** Średni odstęp czasu, po którym następował nawrót wola prawdziwy i rzekomy (regresja Weibulla)

lobe removal and be bilateral, with sufficiently complete excision of both lobes even if one lobe is not enlarged. In the County Hospital in Opole in J. Pichurski



**Fig. 7.** The percentage of recurrences after primary operations in 1958–2000 depending on the form of substitution therapy (binomial-beta hierarchical model)

Ryc. 7. Odsetek nawrotów własnych po strumektomiach wykonanych w latach 1958–2000 w zależności od stosowanej pooperacyjnej profilaktyki farmakologicznej (model dwumianowy-beta)

the 1970s and mid 1980s, dried thyroid gland (Thyroideum, Polfa) was used as substitution therapy. Research, however, indicated that it does not fully block pituitary thyrotropic function after strumectomy, but only mildly decreases TSH secretion [1, 4, 11, 14]. Because of this, synthetic L-thyroxine was used in subsequent years. Most authors think that treatment with L-thyroxine distinctly decreases the number of recurrences mainly due to its effective reduction of TSH level, which is the key pathogenic factor [1, 2, 4, 10, 11, 14–21]. Treatment with L-thyroxine is well established because TSH levels are elevated after the operation and many other growth factors which

contribute to recurrence can be stimulated by TSH [14]. There are also some authors who think that recurrence is unavoidable no matter what form of prophylaxis is used except when total strumectomy is performed [19, 30].

The authors concluded that treatment with L-thyroxine after the primary operation decreased the number of recurrences. As soon as the diagnosis of goiter is established and there are indications for surgery, the operation should be performed promptly because recurrence is faster in older people. Monitoring after the primary operation should be continued for several years to diagnose recurrence as early as possible.

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