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# Papillary Thyroid Microcarcinoma: Clinical and Pathological Study of 321 Cases

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**A B S T R A C T**

*The primary aim of the study was to investigate microcarcinoma characteristics of aggressivity, multicentricity and metastasis. Though its features are not significantly different from those of other papillary carcinomas, the optimal therapeutic approach continues to be an issue of controversy, most notably appropriate surgical approach and indications for neck dissection. The study is retrospective analysis of 321 microcarcinoma cases, operated upon with total thyroidectomy, with or without neck dissection. These cases were compared to larger papillary cancers. We found that 35.1% tumors were aggressive; 25.2% were multicentric, with foci in the contralateral lobe nearly twice as often as in the ipsilateral lobe; and 18.2% were metastatic. In comparison to groups of ≤2 cm and ≤3 cm, microcarcinomas were less aggressive, multicentric and metastatic. Male gender and age <45 were unfavorable parameters. Multivariate analysis revealed contralateral lobe multicentricity and male gender as risk factors for metastasis. Although microcarcinoma demonstrated better characteristics than larger tumors, this subgroup behaves aggressively and should be approached cautiously.*

***Key words:*** *papillary thyroid cancer; microcarcinoma; intraglandular dissemination; regional metastasis; thyreoidectomy*

## Introduction

In recent decades, papillary microcarcinoma has increased in prevalence[1–5]. Nevertheless, this subgroup is subject to many controversies, related to risk assessment, therapeutic approach and follow-up[6–8]. Though microcarcinoma features are not significantly different from those of other papillary carcinomas, the optimal therapeutic approach continues to be an issue of clinical debate, most notably due to the scarcity of sufficiently large prospective studies[9–12]. Ongoing controversies reflect limitations of various prognostic systems, as well as the lack of universally standardized research criteria (inconsistencies in inclusion criteria and well-defined study end-points).

While the optimal surgery for high-risk papillary cancers has already been well established (total thyroidectomy), the approach to low-risk patients, including microcarcinomas, is not as clear[7,13,14]. The appropriate indications for neck dissection, especially elective neck dissection, remain to be determined[15–18]. Low-risk patients (<45 years, $T_1$ tumors, low histological grade, lack of distant metastatic spread) currently represent the largest patient cohort. Recent efforts have attempted to further improve prognosis through selection of a suitable surgical approach and appropriate adjuvant therapy[18]. Some researchers view microcarcinoma as a less aggressive subtype and advocate a minimalist approach, reserving intervention (e.g., lobectomy) for when the tumor turns aggresive[18,19]. In contrast, other studies point to aggressive microcarcinoma behavior and higher incidence of bilateral multicentricity, indicating the need for more aggressive surgery (e.g., near-total thyroidectomy), supplemented by radioiodine ablation[20,21]. Despite the well-recognized characteristics of high-risk papillary cancers, the majority of studies do not provide clear recommendations, putting more importance on excellent prognosis and low incidence of recurrence, focusing on

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the similarities between microcarcinoma and low-risk papillary carcinoma.

There are not many clinical studies aiming to compare tumor size with pathological aggressivity, i.e., intraglandular dissemination and locoregional spread, and analyze other relevant clinical parameters (choice of therapy and recurrence)[22,23]. Tumor aggressivity (nuclear atypia, necrosis, lymphovascular invasion) correlates with metastatic spread, independently from tumor size[23]. Consequently, histological grade should be viewed as prognostically important and set as an obligatory component of any classification system[24].

The primary aim of this study was to investigate selected risk variables (tumor size and aggressivity, multicentricity, locoregional spread, age and sex) for microcarcinoma and larger tumors, primarily up to 3 cm. We elaborated several hypotheses: microcarcinoma is prone to development of multicentric foci and locoregional spread; multicentricity is not related to size or tumor aggressivity, and aggressivity and metastatic spread are linked to age and sex (younger patients and male patients exhibit more aggressive tumors).

## Materials and Methods

This study is a retrospective analysis of clinical and pathological data from 714 patients with the diagnosis of papillary thyroid cancer, both sexes, ages 10–86. There were 321 microcarcinomas. Patients' data are summarized in Table 1. All patients were operated upon at the Department of Otolaryngology–Head and Neck Surgery, »Sestre milosrdnice« University Hospital Center, Zagreb, Croatia, during the period of 1980–2008. Total thyroidectomy, with or without neck dissection (paratracheal or some type of lateral neck dissection) was performed on each patient. Data were collected from patient documentation (operative reports, cytological FNAB results, recurrences, additional thyroid diagnosis), pathology reports, and the Hospital Registry for Thyroid Diseases. Postoperatively, we followed Diagnostic and therapeutic guidelines for differentiated thyroid cancer, issued by Croatian Thyroid Society; postoperative diagnostic scintigraphy were performed with 1–3 mCi $^{131}$I. High risk patients were put to 100–200 mCi $^{131}$I ablation without L-T4. Posttherapeutic whole body scintigraphy were performed 5–8 days after $^{131}$I. 6–12 months after, patients were followed up with neck ultrasound, FT4, TSH, Tg, TgA (without L-T4), and afterwards yearly.

**TABLE 1**
DISTRIBUTION OF PATIENTS WITH PAPILLARY THYROID CARCINOMA (ALL SIZES; GROUPS) INCLUDED IN STUDY, OPERATED UPON FROM 1980–2008

| Characteristic | n=714 |
|---|---|
| Age (yrs) | |
| Range | 10–87 |
| Mean | |
| Microcarcinoma (n=321) | 48,7 (SD=13.37; SEM=0.04) |
| ≤2 cm (n=162) | 47,4 (SD=12.17; SEM=0,07) |
| ≤3 cm (n=234) | 48 (SD=14.05; SEM=0.06) |
| <45 yr. | 282 (40.3%) |
| ≥45 yr. | 417 (59.7%) |
| Gender | n=714 |
| Female | 571 (79.97%) |
| Male | 143 (20.03%) |
| Size of primary tumor (cm) | n=619 |
| Range | 0–10 |
| Mean | 1.55 (SD=1.35; SEM=0.002) |
| Microcarcinoma (≤1 cm) | n=321 (51.9%) |
| Other (>1 cm) | n=298 (48.1%) |

All patients were assigned to groups for variables of age, gender, size (diameter) and pathological aggressivity of the primary tumor, multicentric spread, type of neck dissection performed and presence of neck metastases. There were two age groups, younger (<45 years) and older (≥45 years). Separate analysis was performed for microcarcinoma, as well as tumor sizes of ≤2 cm and ≤3 cm. Variables of tumor aggressivity, multicentricity, neck dissection and metastatic spread were measured in three degrees of severity, as determined in pathological and operative reports (Table 2). Finally, the possible influence of other thyroid comorbidities (lymphocytic thyroiditis and nodular goiter) were examined. Statistical analysis of differences with $\chi^2$ test and multivariate logistic regression for measurement of risk factors for metastatic locoregional spread (gender, age, expansive tm growth and additional diagnosis) were performed. The statistical significance level was set at $p \leq 0.05$.

## Results

There were 321 microcarcinoma tumors (≤1 cm), representing 51.85% of all cases. Rising microcarcinoma prevalence has been demonstrated during the period from 1980–1990, 1991–2000, and after the year 2000 (37.1%, 42.9% and 57.1%, respectively). Results showed that 35.1% of tumors were aggressive; 25.2% were multicentric, with foci in the contralateral lobe nearly twice as often as in the ipsilateral lobe; and 18.2% were metastatic. Comparison between microcarcinoma and groups of other primary tumor sizes (≤2 cm and ≤3 cm) is shown in Table 3.

Tumors >1 cm (1–10 cm) showed significantly more aggressivity (most notably for group III, 24% *vs.* 7.5%). This group displayed more ispilateral and contralateral multicentric foci. More neck dissections (paratracheal and lateral) were performed in the group of large tumors, which also displayed more metastatic spread (paratracheal and lateral). Tumors in the ≤3 cm group (second largest subgroup) were also significantly more aggressive and demonstrated more propensity for multicentric spread than microcarcinoma. More neck dissections were performed and more metastatic foci were found in this

**TABLE 2**
VARIABLES USED IN STUDY; GRADATION BY SEVERITY OF PATHOHISTOLOGICAL FEATURES OF PPRIMARY TUMOR AGGRESSIVITY, INTRAGLANDULAR DISSEMINATION AND LOCOREGIONAL METASTATIC SPREAD

| Gradation | Variables | | | |
|---|---|---|---|---|
| | Pathological aggressivity of primary tumor | Intraglandular dissemination (multicentricity) | Neck dissection* | Locoregional metastatic spread* |
| Grade I | Sharply demarcated; encapsulated | No multicentric foci | Not done | No metastatic spread |
| Grade II | No clear tumor border; tumor capsule invasion | Ipsilateral lobe spread | Paratracheal | Paratracheal metastasis |
| Grade III | Perivascular, perineural spread; tumor necrosis, atypical cells; thyroid capsule invasion; penetration of adjacent soft tissues; fat tissue, muscle, cartilage invasion | Contralateral lobe spread | Lateral | Lateral metastasis |

* Neck dissection classification from: Robbins KT, Shaha AR, Medina JE, et al.: Consensus Statement on the Classification and Terminology of Neck Dissection. Arch Otolaryngol Head Neck Surg. 2008;134:536–538.

**TABLE 3**
COMPARISON OF MICROCARCINOMA *VS*. LARGER PAPILLARY CANCERS (ALL TUMORS, ≤3 CM, ≤2 CM)

| Characteristic | Primary tumor size groups | | | | | | |
|---|---|---|---|---|---|---|---|
| | ≤ 1 cm | 1–10 cm | | ≤3 cm | | ≤2 cm | |
| Tumor aggressivity | 112/319 (35.1%) | 172/293 (58.7%) | p=0.0000 | 130/234 (55.5%) | p=0.0000 | 86/163 (52.7%) | p=0.0007 |
| Tumor capsule invasion | 88 (27.6%) | 100 (34.1%) | | 84 (35.9%) | | 64 (39.2%) | |
| Wider aggression | 24 (7.5%) | 72 (24.6%) | | 46 (19.6%) | | 22 (13.5%) | |
| Multicentric spread | 80/317 (25.2%) | 125/290 (43.1%) | p=0.0000 | 99/235 (42.1%) | p=0.0001 | 65/162 (40.1%) | p=0.003 |
| Ipsilateral | 29 (9.1%) | 43 (14.8%) | | 35 (14.9%) | | 25 (15.4%) | |
| Contralateral | 51 (16.1%) | 82 (28.3%) | | 64 (27.2%) | | 40 (24.7%) | |
| Neck dissection | 121/319 (37.9%) | 145/296 (49%) | p=0.01 | 118/236 (50%) | p=0.016 | 79/164 (48.2%) | p=0.096 |
| Paratracheal | 88 (27.6%) | 96 (32.4%) | | 83 (35.2%) | | 58 (35.4%) | |
| Lateral | 33 (10.3%) | 49 (16.6%) | | 35 (14.8%) | | 21 (12.8%) | |
| Metastatic spread | 58/318 (18.2%) | 92/296 (31%) | p=0.001 | 71/236 (30.1%) | p=0.005 | 47/163 (28.8%) | p=0.02 |
| Paratracheal | 31 (9.8%) | 46 (15.5%) | | 38 (16.1%) | | 28 (17.1%) | |
| Lateral | 27 (8.4%) | 46 (15.5%) | | 33 (14%) | | 19 (11.7%) | |

group as well. The third largest subgroup (≤2 cm), accounting for 26.5% of all papillary carcinomas, also behaved significantly more poorly than microcarcinoma, showing more aggressivity and tendency for multicentric spread. There were no differences in the number of neck dissections performed (p=0.096); differences in metastatic behavior were only marginally significant (p=0.02).

More microcarcinomas were found in the older age group (63.3%). No age differences were found for parameters of pathological aggressivity (p=0.48), multicentricity (p=0.24), or neck dissection (p=0.49). Younger patients had more paratracheal metastasis (15.2% *vs*. 7.5%), and older patients displayed more lateral metastasis (9.1% *vs*. 7,7%), but this difference was only marginally significant (p=0.09, Table 4). In males, tumors behaved significantly more aggressively (p=0.03), with no difference in multicentricity (p=0.79). Males were more likely to undergo lateral neck dissection (15.2% *vs*. 9.5%), and females were more likely to undergo paratracheal neck dissection (27.8% *vs*. 26.1%). Overall, no difference in neck dissection was observed between the groups (p=0.50). Furthermore, males had more metastatic foci (p=0.05) and more paratracheal and lateral metastasis (Table 5).

**TABLE 4**
COMPARISON OF PATHOLOGICAL PARAMETERS BY AGE GROUPS (<45 YEARS, ≥45 YEARS)

| Characteristic | Age <45, n=117 (36.7%) | Age ≥45, n=202 (63.3%) | p |
|---|---|---|---|
| Tumor aggressivity | 44/117 (37.6%) | 67/202 (33.2%) | p=0.48 |
| Tumor capsule invasion | 33 (28.2%) | 55 (27.2%) | |
| Wider aggression | 11 (9.4%) | 12 (5.9%) | |
| Multicentricity | 29/117 (24.8%) | 51/200(25.5%) | p=0.24 |
| Ipsilateral lobe | 14 (12%) | 15 (7.5%) | |
| Contralateral lobe | 15 (12.8%) | 36 (18%) | |
| Neck dissection | 49/117 (41.9%) | 72/200 (36%) | p=0.49 |
| Paratracheal | 37 (31.6%) | 51 (25.5%) | |
| Lateral | 12 (10.3%) | 21 (10.5%) | |
| Metastatic spread | 26/117 (22.2%) | 32/199 (16.1%) | p=0.09 |
| Paratracheal | 17 (14.5%) | 14 (7%) | |
| Lateral | 9 (7.7%) | 18 (9.1%) | |

Hashimoto thyroiditis and nodular goiter were more prevalent in females, but this trend was not significant (p=0.18 and p=0.71, respectively).

**TABLE 5**
COMPARISON OF PATHOLOGICAL PARAMETERS BY AGE GROUP

| Characteristic | Males, n=47 (14.6%) | Females, n=274 (85.4%) | p |
|---|---|---|---|
| Tumor aggressivity | 23/47 (48.9%) | 89/272 (32.7%) | p=0.03 |
| Tumor capsule invasion | 18 (38.3%) | 70 (25.7%) | |
| Wider aggression | 5 (10.6%) | 19 (7%) | |
| Multicentricity | 11/46 (23.9%) | 69/271 (25.5%) | p=0.79 |
| Ipsilateral lobe | 3 (6.5%) | 26 (9.6%) | |
| Contralateral lobe | 8 (17.4%) | 43 (15.9%) | |
| Neck dissection | 19/46 (41.3%) | 102/273 (37.4%) | p=0.50 |
| Paratracheal | 12 (26.1%) | 76 (27.8%) | |
| Lateral | 7 (15.2%) | 26 (9.5%) | |
| Metastatic spread | 13/46 (28.3%) | 45/272 (16.5%) | p=0.05 |
| Paratracheal | 8 (17.4%) | 23 (8.5%) | |
| Lateral | 5 (10.9%) | 22 (8%) | |
| Additional diagnosis | | | |
| Hashimoto disease | 7/47 (14.9%) | 65/274 (23.7 %) | p=0.18 |
| Nodular goiter | 15/47 (31.9%) | 95/274 (34.7 %) | p=0.71 |

Multivariate analysis of parameters of gender, age, expansive tm growth and additional diagnosis revealed the presence of multicentric foci in both lobes to be an independent risk factor for locoregional metastatic spread (OR 2.427), while nodular goiter was identified as a protective factor (OR 0.453). Tumor aggressivity was not identified as predictive of locoregional metastatic spread (Table 6). Age and sex were not identified as important risk factors.

**TABLE 6**
RISK FACTORS FOR REGIONAL METASTATIC SPREAD, LOGISTIC REGRESSION MODEL

| | OR | 95% CL | | p |
|---|---|---|---|---|
| | | Upper | Lower | |
| Gender | | | | |
| Male | 1.987 | 0.97 | 4.08 | 0.0614 |
| Female | 0.503 | 0.24 | 1.03 | 0.0614 |
| Age (years) | 0.976 | 0.95 | 1.00 | 0.0284 |
| Older (45 and older) | 0.671 | 0.38 | 1.20 | 0.1758 |
| Multicentricity | | | | |
| No multicentric spread | 0.636 | 0.34 | 1.18 | 0.1523 |
| Ipsilateral | 0.487 | 0.14 | 1.67 | 0.2524 |
| Contralateral | 2.427 | 1.23 | 4.79 | 0.0107 |
| Expansive tm growth | | | | |
| No expansion | 0.801 | 0.45 | 1.44 | 0.4591 |
| Tumor capsule invasion | 1.209 | 0.65 | 2.25 | 0.5500 |
| Wider aggression | 1.187 | 0.42 | 3.33 | 0.7446 |
| Additional diagnosis | | | | |
| Hashimoto disease | 1.295 | 0.67 | 2.51 | 0.4434 |
| Nodular goiter | 0.453 | 0.23 | 0.90 | 0.0240 |

## Discussion

There has been a large volume of papillary microcarcinoma research on the important clinicopathological features of this increasingly encountered subtype of thyroid cancer. Research efforts have sought to differentiate this tumor subtype from larger papillary tumors, as measured by parameters of primary tumor aggressivity, metastatic potential and affinity for locoregional recurrence. Consensus regarding the optimal therapeutic protocol would have great impact on the clinical approach as well as the postoperative follow-up regimen. In this study, we tried to investigate several pathological and clinical characteristics with which to differentiate papillary cancers not belonging to the microcarcinoma group (>1 cm). The majority of papillary carcinomas presented in this study were microcarcinomas (51.9%). The most notable rise in prevalence rise (57.1%) was observed during the last decade of study (2001–2008), thereby identifying microcarcinoma as the most commonly presented tumor. This trend of increasing incidence has recently been reported elsewhere[4,7]. It is generally accepted that microcarcinomas belong to a separate, less aggressive subgroup of papillary cancers, which exhibit a tendency for benign clinical behavior and therefore demand a less aggressive approach. Cheema et al. report excellent disease prognosis with low recurrence rates (8%) and 100% survival, attributing favorable results to an initial aggressive approach (total thyroidectomy in 80% of cases, accompanied by neck dissection in the case of clinically significant regional metastatic disease)[20].

In contrast, histological grading has been found prognostically superior to tumor subclassification for evaluation of papillary carcinoma[24]. Characteristics such as nuclear atypia, tumor necrosis and lymphovascular invasion are all identified as important factors in evaluation of tumor aggressivity, recurrence risk, and metastatic dissemination. For these reasons, we chose tumor aggressivity, multicentricity and metastatic spread as important clinicopathological variables of papillary cancer to be measured in our study. We found microcarcinoma aggressivity in 35.1% of cases. Most aggressivity was in the form of the absence of a sharp tumor demarcation and/or tumor capsule invasion (more than two-thirds of all aggressive cases), and less commonly, wider aggression (7.5%). Microcarcinomas demonstrated significantly less aggressivity than tumors >1 cm (1–10 cm), and slightly less in comparison with the ≤2-cm and ≤3-cm subgroups (both groups had aggressive characteristics in more than half of the cases). Nonetheless, it can be postulated that microcarcinoma aggressivity, found in more than one third of cases, demonstrates signifficant cinical finding, pointing to similar behaviour as other larger tumors. In contrast to other reports, we distinguished the gradation of primary tumor aggressivity by differentiating tumor capsule invasion (grade II) from thyroid gland capsule invasion (grade III).

Multifocality is a well-known characteristic of papillary cancer, present in 24–30% of cases[20,21]. This study demonstrated 25.2% prevalence of multicentric tumors,

which is in concordance with literature reports. Multicentric intrathyroid dissemination suggests a higher propensity for locoregional spread and higher recurrence risk[6]. At the same time, the presence of multiple foci correlates with detailed systematic pathological examination of thyroid specimens. There are major disagreements about the significance of multicentricity in papillary cancer and microcarcinoma, as well. Many authors, aware of its high prevalence in both thyroid lobes, advocate total thyroidectomy as an operation of choice, stating that more extensive operations decrease the likelihood of recurrence[26]. On the other hand, several larger multivariate analyses have not identified multicentricity as a risk factor for recurrence. However, a clear connection between the presence of multicentricity and metastatic spread has arguably been revealed. For microcarcinoma, the importance of multicentricity remains to be investigated effectively, reflecting the problem of clinical material diversity, inconsistencies in initial therapeutic approach and less than detailed pathological examination. Baudin et al. suggest two important parameters with impact on recurrence: number of histological foci and extent of initial operation. The authors recommend that decisions regarding the extent of surgery should be based on multifocality findings (i.e., lobectomy in cases of single tumor focus and total thyroidectomy plus central neck dissection for multifocal tumor)[18]. Our study revealed that 25.2% of microcarcinomas developed multicentric foci, with most appearing in the contralateral lobe (16.1%). Thus multicentricity, when it occurs, is bilateral in more than 60% of multicentric cases. This fact should be seen in light of earlier studies reporting more extensive operations (total thyroidectomy *vs*. lobectomy) leading to reduced rate of recurrence, 5% *vs*. 20%, respectively[18]. On multivariate analysis, multicentricity was found to be the single most important risk factor for development of metastatic spread (OR 2.427). Even stronger association was evident for tumors >1 cm (OR 3.119). In both cases, the correlation applies to the presence of one or more multicentric foci in the contralateral lobe. Interpretation of this finding strongly signifies the need for an initially cautious surgical approach, incorporating complete removal of the contralateral lobe in suspicious cases. We should underline that this surgical approach (total thyroidectomy) has been part of our surgical protocol throughout the entire period of study, significantly contributing to quality analysis of intraglandular tumor spread.

Locoregional metastatic spread is one of the most important risk factors preceding distant dissemination, with reported frequency of 3.1–18.2%[27,28]. We found that microcarcinoma are prone to metastatic behavior, with prevalence of 18.2%. In 53% of cases, the paratracheal region was the only site of metastatic growth; lateral regions were involved in 47% of cases. The distribution of locoregional spread followed well-known pathways of lymphatic drainage, with the paratracheal region being involved most commonly. Even though we found that microcarcinoma exhibited significantly less metastatic potential, we have demonstrated that regional metastatic spread is directly dependent on tumor size, without a clear-cut size margin. This observation once again addresses the importance of preoperative neck diagnostics and careful intraoperative neck exploration. We also found that the chance of metastatic spread is increased in cases of multicentricity by more than two-fold. Our findings basically agree with those reported by Hay et al., emphasizing higher relative recurrence risk for metastasizing papillary carcinomas[29].

Patient age is an important independent prognostic predictor, incorporated in TNM as well as many other classification systems, marking patients less than 45 years of age as low risk and patients older than 45 as a high risk[30]. In the present study, we demonstrated relatively worse behavior in the younger group, across all of the measured variables, except for multicentricity. Tumors in the younger subpopulation were slightly more aggressive, with no statistical significance (37.6% *vs*. 33.2%, p=0.48). Differences between age groups became more evident when metastatic potential was examined, with the younger group having a higher frequency of metastatic spread (22.2% *vs*. 16.1%, p=0,09). This somewhat higher aggressivity in the younger group does not necessarily represent worse prognosis in terms of specific survival, more commonly present in the older population[31]. We confirmed these findings in larger tumors as well, a finding that was generally not in accordance with the majority of other studies, which found more aggressivity among the older population[25]. Regarding gender, microcarcinoma pathological aggressivity (48.9% *vs*. 32.7%), as well as metastatic dissemination in all neck regions (22.7% *vs*. 16,1%) were significantly worse parameters in males, while multicentricity was similar in males and females. These differences were even more evident among patients with larger tumors. This is in accordance with the relatively low number of related studies that have demonstrated gender as an independent risk factor for recurrence and identified the prognostic importance of male gender (higher estimated risk for multiple recurrences and unsuccessful salvage surgery)[32,33].

To date, many multivariate studies on papillary carcinomas have been published in an attempt to analyze the impact of potentially important prognostic factors. The most commonly differentiated factors are age, tumor grade and extension (extrathyroid invasion, distant metastases, and, less commonly, regional metastases). Several scoring systems have evolved, in an effort to stratify prognostic risk between low- and high-risk patients. The spectrum of recommended surgical options for microcarcinoma is broad, including total thyroidectomy, near-total thyroidectomy, subtotal thyroidectomy and lobectomy with isthmusectomy. The most minimal approach is clinical observation and periodical follow-up, with indications for therapeutic intervention only when the tumor turns more aggressive[34]. The American Thyroid Association advises lobectomy for small, low-risk cancers without metastatic spread, while total thyroidectomy is advised for cases of multifocality and metastatic spread. The

British Thyroid Association made similar recommendations[35–37]. However, some authors favor a more aggressive approach to microcarcinoma (total thyroidectomy accompanied by ablative therapy), similar to the approach used for other, larger tumors. Some investigators suggest that tumors with unusual microscopic characteristics, capsule invasion, lymphovascular extension or tall-cell subtype should be included in separate groups. Such authors assert increased aggressivity to be more frequent in patients of younger age and male sex, as demonstrated in our study. In summary, microcarcinomas show clinicopathological characteristics that do not separate them exclusively from other papillary carcinomas[38]. We do not support the claim that more aggressive surgery (total thyroidectomy) is associated with more morbidity, because perioperative morbidity was very low (below 1%). Further, the fact that multicentric tumors, when they occur, arise in the contralateral lobe in 60% of cases, point to the need to extend surgery to the other lobe, thereby eliminating the most common site of possible future recurrence. With high incidence of paratracheal and lateral metastasis, it is necessary to perform meticulous intraoperative neck exploration in search of suspicious lymph nodes and to perform neck dissection (paratracheal and/or lateral) at the same time as thyroid gland surgery, when deemed necessary. Future research should elucidate the precise therapeutic guidelines to be used for this commonly encountered thyroid tumor.

## Conclusion

Even though our study identified microcarcinoma as a tumor with clinical and pathological characteristics better to those of larger tumors, we can conclude that papillary thyroid microcarcinoma behaves aggressively, in many ways, primarily in comparison with tumors up to 3 cm, and therefore recommend a cautious clinical approach.

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## PAPILARNI MIKROKARCINOM ŠTITNJAČE: KLINIČKA I PATOLOŠKA STUDIJA 321 SLUČAJA


### S A Ž E T A K

Osnovni cilj studije bio je istražiti patološku agresivnost, multicentričnost i metastatske osobitosti papilarnog mikrokarcinoma štitnjače. Postavljene su hipoteze da je mikrokarcinom sklon pojavi multicentričnih žarišta tumora i lokoregionalnom širenju; multicentričnost nije povezana sa veličinom niti agresivnošću tumora; agresivnost i metastatsko širenje povezano je sa dobi i spolom. Metode: retrospektivna analiza 321 slučaja mikrokarcinoma, operiranih totalnom tireoidektomijom sa ili bez disekcije vrata. Svi slučajevi usporedjeni su sa papilarnim karcinomima veće veličine primarnog tumora. Rezultati: 35,1% tumora je bilo agresivno; 25,2% je pokazalo multicentričnost, sa žarištima u kontralateralnom režnju približno dvostruko češće nego u ipsilateralnom režnju; 18,2% tumora je metastaziralo lokoregionalno. U usporedbi sa odvojenom grupom tumora od ≤2 cm and ≤3 cm, mikrokarcinomi su bili manje agresivni, multicentrični i metastatski. Muški spol i dob <45 godina pokazani su kao nepovoljni klinički parametri. Multivarijantna analiza pokazala je postojanje multicentričnih žarišta u kontralateralnom režnju te muški spol kao rizične čimbenike za pojavu metastaza. Zaključak: premda je mikrokarcinom u ovoj studiji pokazao bolje kliničko ponašanje od papilarnih karcinoma veličine veće od 1 cm, ova podgrupa tumora ponašala se značajno agresivno te savjetujemo nužni oprez u kliničkom pristupu ovoj značajnoj podgrupi pacijenata.