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# 부신 우연종 환자의 적합한 치료 방향 결정에 관여하는 예후 예측 인자 분석

Analysis of Prognostic Predictors Associated with Determining Appropriate Treatment Direction for Patients with Adrenal Incidentaloma

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**Abstract**

***Introduction:*** Adrenal incidentaloma is mostly nonfunctional and benign, mostly detected during other medical examinations. Computed tomography (CT) findings help the detection and differential diagnosis of such tumor. Functional and malignant tumors are indicated for surgical treatment. Nonfunctioning adrenal incidentaloma usually undergoes regular follow-up. However, in certain patients, they may require treatment such as adrenalectomy to receive appropriate treatment even with the nonfunctional adrenal incidentalomas. This study aims to evaluate the prognostic predictors associated with determining appropriate treatment direction in patients with adrenal incidentaloma.

***Materials and Methods:*** This is a retrospective, single tertiary center study in patients with nonfunctioning adrenal incidentaloma diagnosed from January 2000 to December 2020. Patients were divided into two groups; surgery group and observation group. Then, subgroup analysis was performed between malignant and benign adenoma patients in the surgery group. Baseline characteristics, biochemical test results, CT findings and pathologic results of surgery group were collected. Also, CT scan findings associated with malignant potential features such as tumor size, Hounsfield unit (HU) and washout values were measured and calculated.

***Results:*** Of all, 307 patients were included in this study, with 127 patients in surgery group and 180 patients in observation group. Surgery group was younger and had larger tumor size compared to observation group ($p<0.05$). The most common reason for adrenalectomy in surgery group was tumor size 4 cm or larger (35.4%) at the time of diagnosis, while 25.2% of patients had tumor size increase during the follow-up as a reason for surgery. Regarding CT findings, surgery group presented certain morphological features and malignant potential features more than observation group. Dominant pathologic results in surgery group were adrenal cortical adenoma (25%), followed by metastatic carcinoma (14%). Within the surgery group, mean tumor size was less than 4 cm in both malignancy group and adenoma group (3.79 cm and 3.05 cm, respectively, $p=0.645$). Malignant group showed more irregular border on CT, having more patients with absolute washout less than 60% and relative washout less than 40% than adenoma group.

***Conclusion:*** Characterization of nonfunctioning adrenal incidentaloma is important to provide appropriate treatment for adrenal incidentaloma patients since every adrenal incidentaloma does not present favorable prognosis. Findings of CT scan associated with malignant potential such as HU and washout values were supportive to decide the need of surgical treatment.

However, conventional size criteria of 4 cm or larger for surgery was not reliable to predict malignancy in this study. Surgical resection of adrenal incidentalomas should be considered in certain group of patients presenting aforementioned factors to receive appropriate treatment rather than observation.

**Keywords**: Nonfunctioning adrenal incidentaloma, Hounsfield unit, Washout, Dynamic CT

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## Introduction

Adrenal incidentaloma is an adrenal tumor detected incidentally by radiologic imaging, performed for other medical indications than adrenal diseases. Prevalence of adrenal incidentaloma varies by reports, from 1 to 6%, with a peak in fifty to seventies [1]. Since technology and usage of computed tomography (CT) imaging has increased, the detection of adrenal incidentaloma has been gradually increasing [2]. It is known to be found in 4.4-5% of CT scans [3, 4]. Most adrenal incidentalomas are known to be nonfunctioning, benign tumors rather than being hormone-producing or malignant [1, 3, 5]. In Korea, single-center report has shown that older people have higher incidence of adrenal incidentaloma detected, and among the adrenal incidentaloma, 13.8~17.8% were functioning tumors [2, 6].

Even if an adrenal incidentaloma is initially evaluated to be nonfunctioning and benign, there is a possibility of tumor growth and transition to functional tumor during the follow-up. Therefore, regular and long-term follow-up for is recommended for patients with adrenal incidentaloma [7]. Since standard treatment for hormone-producing adenoma or malignant adrenal tumor is surgical resection, thorough evaluation to characterize adrenal incidentaloma is crucial [8]. In addition, the majority of adrenal incidentalomas discovered in patients with history of extra-adrenal malignancies has been found to be benign rather than metastasis of primary cancers which would have not required adrenalectomy [9]. Moreover, clinical significance of nonfunctioning adrenal incidentalomas, especially regarding cardiometabolic diseases, is emerging nowadays. Nonfunctioning adrenal incidentalomas are found to be related to higher risk for diabetes and hypertension, and surgical resection resulted in yield of resolution of hypertension [10, 11, 12]. Therefore, it is important to evaluate the characteristics of adrenal incidentaloma when detected.

For differential diagnosis of adrenal incidentaloma, certain features in CT scan that characterize the tumor have been suggested. Attenuation of adrenal tumor measured in pre-contrast CT scan less than 10 Hounsfield units (HU) suggests an adrenal tumor to be benign [13]. Also, the concept of washout value calculated in contrast-enhanced CT has been applied to characterize adrenal incidentalomas, with absolute and relative washout less than 60% and 40%, respectively, suggesting malignant nature of an incidentaloma [14]. Moreover, homogeneity and smooth border were studied as indicators of benign adrenal tumor, but did not show satisfying result [15].

Management of nonfunctioning adrenal incidentaloma subtly varies by guidelines. Tumor size equal to or larger than 4 cm is usually applied as a surgical indication, and others are

suggested to regular follow-up [16]. Regarding nonfunctioning adrenal incidentaloma with size smaller than 4 cm in diameter, follow-up imaging is even not indicated if its attenuation is <10 HU, unless any clinical presentation related to hormonal excess develops [1].

Although there have been retrospective studies on clinical characteristics of adrenal incidentaloma in Korean patients, there are insufficient reports that compare the patients with nonfunctioning adrenal incidentaloma that underwent surgery with patients on observation. In this study, we investigated the clinicopathologic characteristics of patients with nonfunctioning adrenal incidentalomas, aiming to detect the prognostic predictors associated with determining appropriate treatment direction by comparing surgery group and observation group.

## Materials and Methods

*Subject*

This study is retrospective, single tertiary center study carried out in patients diagnosed as nonfunctioning adrenal incidentaloma in Asan Medical Center from January 2000 to December 2020. Patients either underwent adrenalectomy or observation since the time of diagnosis. In surgery group, patients who had adrenal biopsy before surgery were excluded. Patients who were lost or found to have functional transformation during follow-up, and patients with insufficient data (i.e. no follow-up CT scan) were excluded from observation group.

*Data collection*

Baseline characteristics such as age, sex, underlying diseases and body mass index (BMI) of each patient were collected by review of electronic medical records. For the surgery group, reason for CT evaluation and surgery, and final pathologic results were collected. Regarding CT images, basic characters of adrenal tumor such as size, side and malignant potential features were collected. Several features frequently noted in CT scan reports, such as calcification and irregular borders, were chosen as variables. When the maximum diameter of adrenal tumor size measured at the same image level between the initial CT and follow-up CT scans increases, it was considered as having a change of tumor size.

*Preoperative CT scan findings*

Contrast-enhanced adrenal CT or abdominal CT scan was performed, and the washout of intravenous contrast medium was calculated at 60 to 90 seconds (portal venous phase) and at 10 to 15 minutes (delayed enhancement phase) after contrast administration. To calculate the washout of intravenous contrast medium for the tumor, HU was measured during the pre-contrast phase, portal venous phase, and delayed phase. Absolute washout was calculated as the difference between the attenuation value in the HU in an early enhanced CT and the HU on a delayed CT image. This difference was divided by the HU difference between the early enhanced CT and an unenhanced CT image, and the result was then multiplied by 100%. Relative washout was calculated by subtracting the HU on a delayed CT image from the HU on an early enhanced CT image. The resulting value was divided by the HU on the enhanced CT image and then multiplied by 100% [7]. The adrenal tumor size was measured by identifying the longest diameter of the tumor on the image displaying the largest lesion area in

the cross-sectional view of the CT scan. The malignant features in CT scan was defined as tumor size ≥4 cm, pre-contrast HU ≥10, absolute washout <60%, and relative washout <40% [17]. If patients did not have adrenal CT record, only pre-contrast attenuation was measured and recorded.

*Statistical analysis*

Categorical variables were expressed as numbers and percentage, and analysis was done by Chi-square test and Fisher's exact test. Continuous variables were noted as mean and standard deviation (SD), analyzed by Student t-test and median with range by Mann-Whitney U test. All analyses were conducted with SPSS statistics 21.0 (IBM Corporation, Armonk, NY, USA). P value smaller than 0.05 was considered significant.

## Results

*Baseline characteristics of patients*

During the study period, 744 patients were diagnosed adrenal incidentaloma (Figure 1). Among them, 130 patients underwent surgery and 614 patient were followed up without surgery. In surgery group, 3 patients who had biopsy before surgery were excluded. Regarding observation group, total of 434 patients were excluded by following reasons; 181 patients lost during follow-up, 168 patients newly diagnosed as functional adenoma during follow-up, and 85 having insufficient data for analysis. In final, 127 patients and 180 patients were included in surgery group and observation group, respectively.

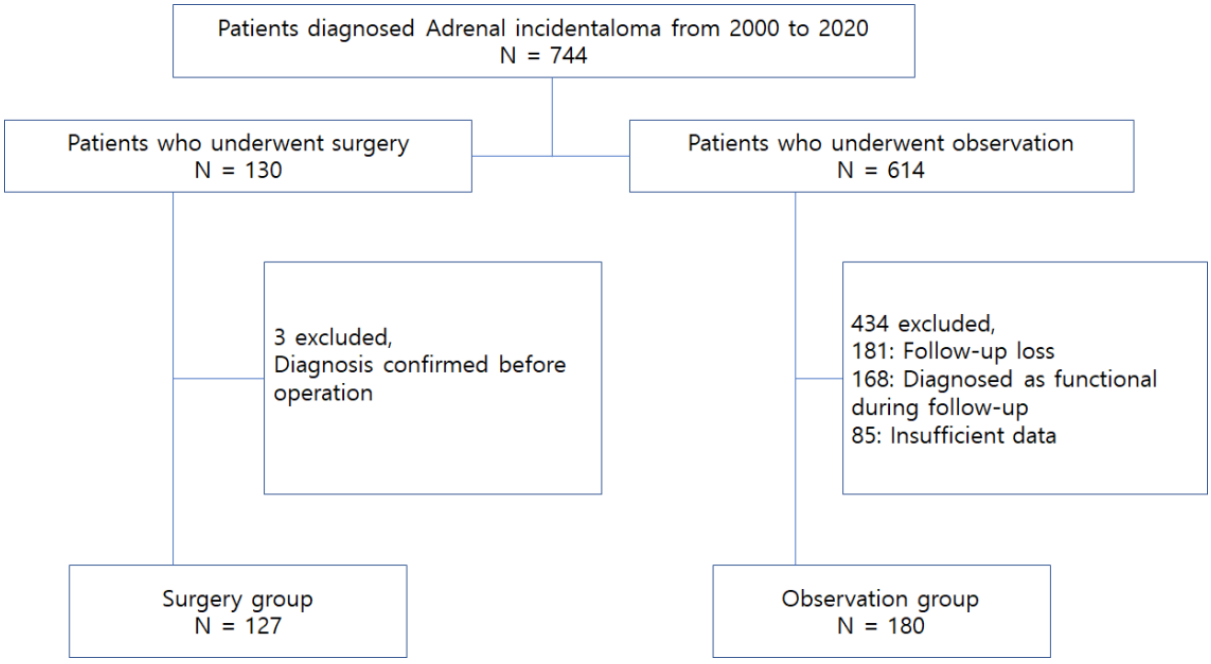


**Figure 1.** Flowchart diagram of the study subjects.

Clinical characteristics between surgery and observation groups are shown in Table 1. The age of surgery group was younger than that of observation group (p=0.003). Regarding reason of performing CT scan, in surgery group, 48 (37.8%) patients had CT for general medical examination, 13 (10.2%) for abdominal or flank pain workup, 5 (3.9%) for gastrointestinal symptoms, and 2 (1.6%) because they had palpable mass. And, 21 (16.5%) patients took CT as work up for other benign diseases, while for 17 (13.4%) it was for malignant diseases work up. Lastly, 21 (16.5%) patients took CT for regular follow-up of their underlying diseases. In observation group, 57 (31.7%) patients had CT for general examination, 11 (6.1%) because

they had abdominal or flank pain, 3 (1.7%) due to gastrointestinal symptoms. For the rest, 35 (19.4%) took CT for benign diseases work up, while 58 (32.2%) for evaluation of malignant diseases, and finally 16 (8.9%) as means of regular follow-up of underlying diseases.

**Table 1.** Clinical characteristics between surgery group and observation group.

| | Surgery group (n=127) | Observation group (n=180) | ***p*-value** |
|---|---|---|---|
| Sex (%) | | | 0.244 |
| Male | 67 (52.8) | 107 (59.4) | |
| Female | 60 (47.2) | 73 (40.6) | |
| Age at diagnosis, years (mean±SD) | 53.18 (±14.46) | 58.2 (±10.25) | 0.003 |
| BMI (mean±SD) | 24.56 (±4.22) | 25.13 (±3.04) | 0.233 |
| Reason for CT scan (%) | | | 0.001 |
| General medical examination | 48 (37.8) | 57 (31.7) | |
| Abdominal or flank pain | 13 (10.2) | 11 (6.1) | |
| Gastrointestinal symptoms | 5 (3.9) | 3 (1.7) | |
| Palpable mass | 2 (1.6) | 0 (0) | |
| Work up for benign diseases | 21 (16.5) | 35 (19.4) | |
| Work up for malignant diseases | 17 (13.4) | 58 (32.2) | |
| Regular follow up for underlying diseases | 21 (16.5) | 16 (8.9) | |
| Side of tumor (%) | | | 0.084 |
| Left | 83 (65.4) | 114 (63.3) | |
| Right | 43 (33.9) | 56 (31.1) | |
| Bilateral | 1 (0.8) | 10 (5.6) | |
| Underlying diseases (%) | | | |
| Hypertension | 38 (35.8) | 66 (36.7) | 0.219 |
| Diabetes mellitus | 18 (17.6) | 25 (13.9) | 0.944 |
| Dyslipidemia | 8 (8.2) | 18 (10) | 0.251 |
| Prostate cancer | 2 (2.1) | 5 (2.8) | 0.704 |
| Herniated intervertebral disc | 5 (5.3) | 2 (1.1) | 0.130 |
| Benign prostate hyperplasia | 6 (6.3) | 2 (1.1) | 0.069 |

| | | | |
|---|---|---|---|
| Tumor size on CT, cm (mean±SD) | 4.58 (±2.34) | 1.63 (±0.93) | <0.001 |
| Reason for surgery (%) | | | |
| Tumor size ≥ 4 cm | 45 (35.4) | | |
| Tumor size increase | 32 (25.2) | | |
| Atypical feature on CT | 47 (37) | | |
| Abdominal discomfort symptom | 2 (1.6) | | |
| Patient's wish | 1 (0.8) | | |

Underlying diseases of each patient were obtained. In surgery group, 38 (35.8%) patients had hypertension (HTN), 18 (17.6%) had diabetes mellitus (DM), and 8 (8.2%) had dyslipidemia (DL). Two (2.1%) patients had prostate cancer while 6 (6.3%) patients had benign prostate hyperplasia (BPH), and 5 (5.3%) patients had herniated intervertebral disc (HIVD). In observation group, 66 (36.7%) patients had HTN, 25 (13.9%) patients had DM, 18 (10%) patients had DL while 5 (2.8%) had prostate cancer, 2 (1.1%) had BPH and 2 (1.1%) had HIVD.

The mean size of tumor presented on CT scan was 4.6 cm in surgery group and 1.6cm in observation group. Surgery group had significantly larger tumor size measured on CT compared to observation group presenting median of 4.1 cm (range, 1.1 to 11.5 cm) and 1.4 cm (range, 0.5 to 5.4 cm), respectively ($p$<0.001) (Figure 2).

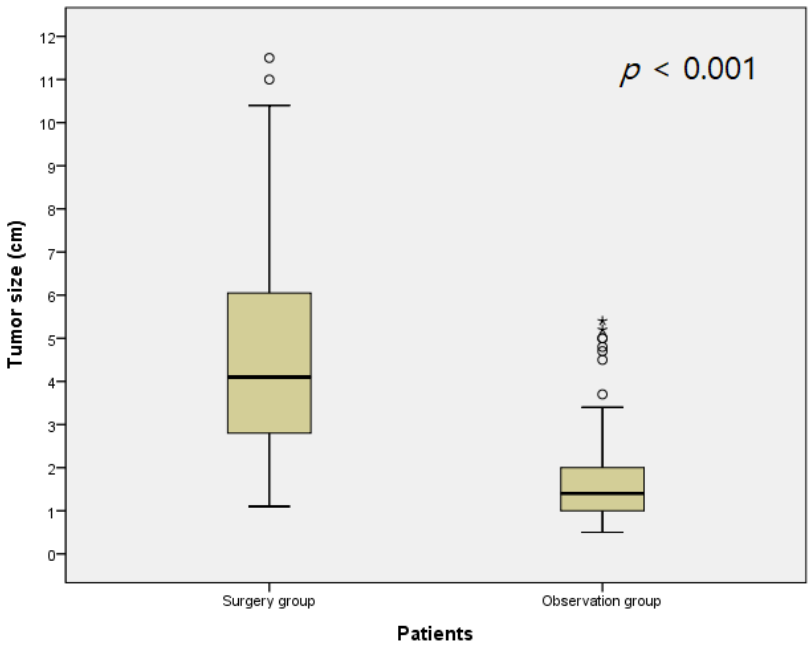


**Figure 2.** Box plot of tumor size between the surgery group and observation group.

There were several reasons for surgery in surgery group. Forty-five patients (35.4%) and 32 patients (25.2%) underwent adrenalectomy because the size of tumor was ≥4 cm, or tumor size increase during follow-up, respectively. Forty-seven patients (37%) underwent surgery because of atypical features on CT images while 2 patients (1.6%) had abdominal discomfort and one patient (0.8%) wished to receive surgery.

*Change of tumor sizes between two groups*

The change of tumor size were measured by follow-up CT images in observation group, 50 patients (28.8%) had increase of tumor size compared to initial diagnosis (Figure 3). Nine patients grew up over 4 cm, however, these patients did not received surgery because their CT features suggested benign nature.

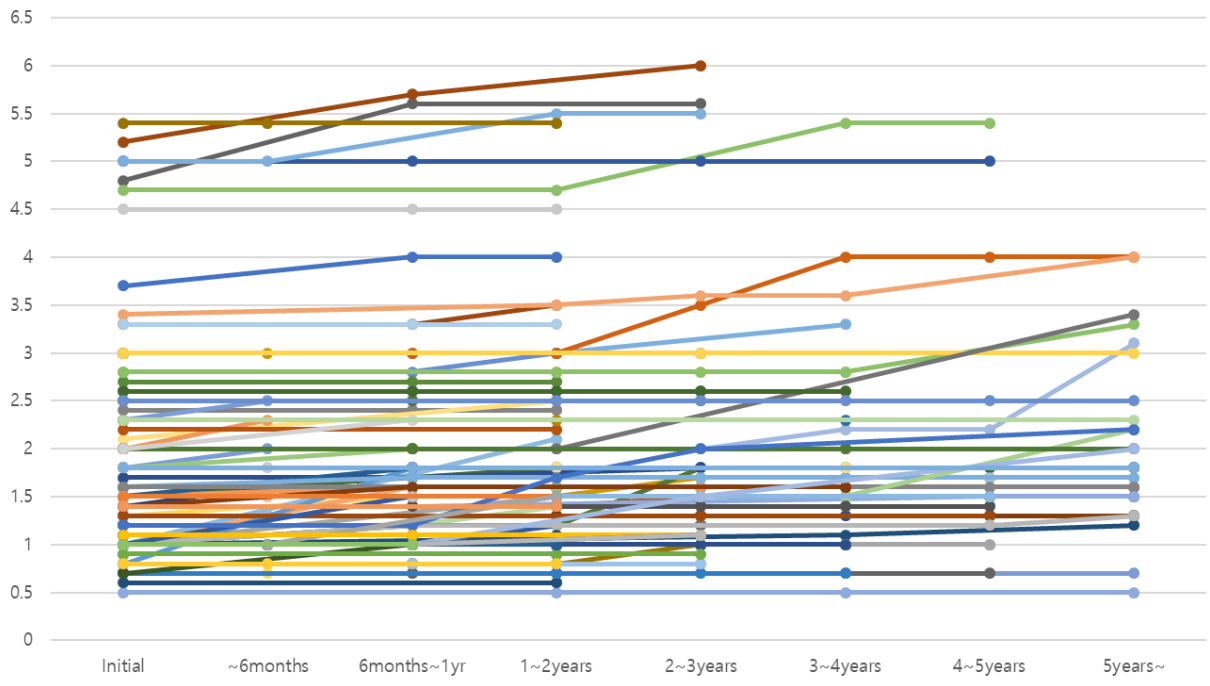


**Figure 3.** Change of the tumor size in observation group (n=50).

In surgery group, 32 patients underwent adrenalectomy for the reason of tumor size increase after the initial evaluation. The mean size increase was 1.5 cm, and the maximum size was 8.8 cm (Figure 4).

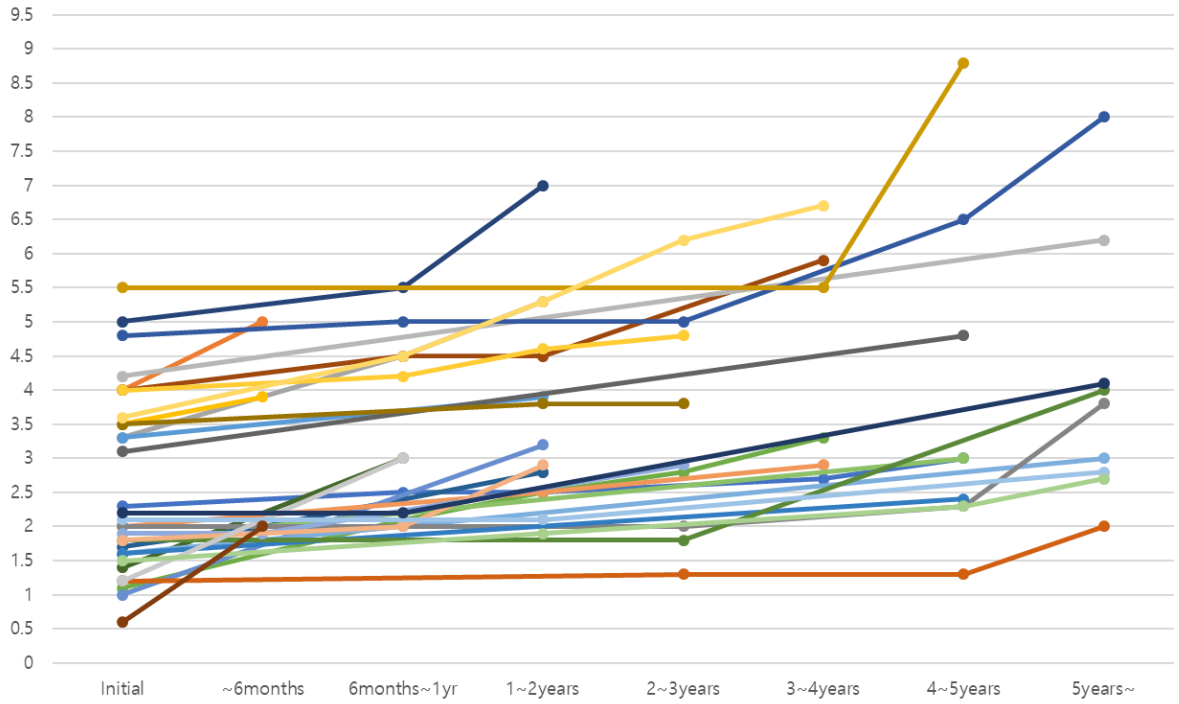


**Figure 4.** Change of the tumor size in surgery group (n=32) who underwent surgery due to size increase.

Characteristics of CT scan are compared between the two groups in Table 2. Regarding morphological features, there are significantly more calcification in surgery group (n=18, 14.2%) compared to observation group (n=7, 3.9%; $p$=0.001). Twenty-nine patients (22.8%) in surgery group had heterogenous enhancement of tumor, while only 3 patients (1.7%) had it in observation group ($p$<0.001). Lastly, 23 patients (18.1%) in surgery group had irregular border, while 10 (5.6%) had in observation group ($p$<0.001). Overall, all morphological features, except overall cystic feature were significantly more frequent in surgery group compared to observation group.

Regarding to the malignant potential features on CT scan, tumor size equal or larger than 4 cm were in 69 patients (54.3%) in surgery group and only 7 patients (3.9%) in observation group ($p$<0.001). In case of pre-contrast attenuation (available in 98 and 171 patients in surgery and observation group, respectively), 85 (86.7%) and 109 patients (63.7%) presented ≥ 10 HU in surgery and observation group, respectively ($p$<0.001). Regarding washout values (available in 93 and 135 patients in surgery and observation group, respectively), patients with absolute washout <60% were more frequent in surgery group (n=73, 78.5%) compared to observation group (n=26, 26.7%; $p$<0.001). There were significantly more patients with relative washout <40% in surgery group (n=74, 79.6%) compared to observation group (n=23, 17%; $p$<0.001).

These findings suggested CT features suggested malignant potential were more frequently founded in surgery group.

**Table 2**. Comparison of computed tomography characteristics between surgery group and observation group.

| | Surgery group (n=127) | Observation group (n=180) | *p*-value |
|---|---|---|---|
| Morphological features (%) | | | |
| Calcification | 18 (14.2) | 7 (3.9) | <0.001 |
| Heterogenous enhancement | 29 (22.8) | 3 (1.7) | <0.001 |
| Fat portion | 17 (13.4) | 9 (5) | 0.009 |
| Overall cystic feature | 12 (9.4) | 9 (5) | 0.128 |
| Internal cystic portion | 6 (4.7) | 0 (0) | 0.005 |
| Irregular border | 23 (18.1) | 10 (5.6) | <0.001 |
| Malignant potential features (%) | | | |
| Tumor size ≥ 4 cm | 69 (54.3) | 7 (3.9) | <0.001 |
| Pre-contrast ≥ 10 HU | 85 (86.7) | 109 (63.7) | <0.001 |
| Absolute washout <60% | 73 (78.5) | 26 (26.7) | <0.001 |
| Relative washout <40% | 74 (79.6) | 23 (17) | <0.001 |

Final pathologic results in surgery group are presented in Figure 5. Of all, 32 patients (25%) were diagnosed of adrenal cortical adenomas and 18 (14%) were metastatic carcinomas. Myelolipma, oncocytoma, and ganglioneuroma were confirmed in 13 (10%), 13 (10%), and 11 patients (9%), respectively. Small number of patients had pheochromocytoma (n=9, 7%), other benign diseases (n=9, 7%), benign cystic diseases (n=8, 6%), hemangioma (n=5, 4%), schwannoma (n=4, 3%), adrenal cortical carcinoma (n=2, 2%), mucinous carcinoma (n=2, 2%), and lymphoma (n=1, 1%).

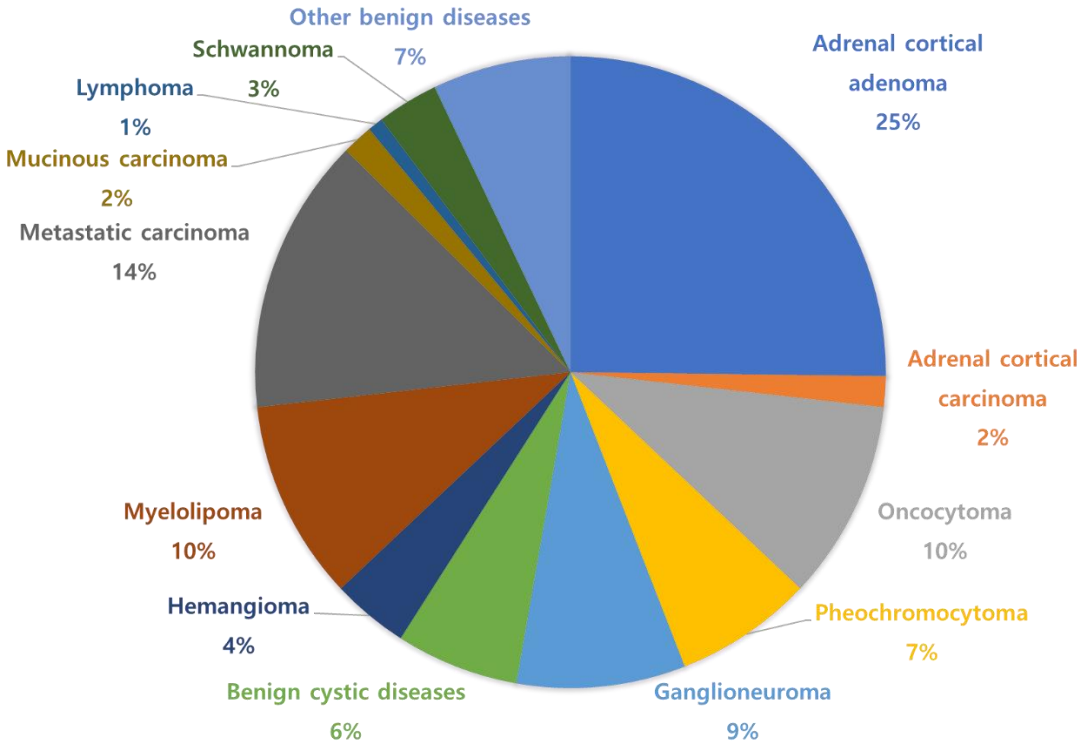


**Figure 5**. Diagram of the final pathologic results in surgery group.

In surgery group, we compared the features of CT scan between malignancy group (n=23) including adrenal cortical carcinoma, metastatic carcinoma, mucinous carcinoma and lymphoma, and benign adenoma group (n=32) as shown in Table 3. We evaluated pre-contrast attenuation (available in 18 and 24 patients in malignancy and adenoma group, respectively) and washout values (available in 16 and 23 patients in malignancy and adenoma group).

The mean tumor size was less than 4 cm in both malignancy group and adenoma group with no statistical difference (3.79 cm and 3.05 cm, respectively, $p$=0.645). Irregular border was more frequent in malignancy group (n=7, 30.4%) compared to the adenoma group (n=1, 3.1%; $p$=0.007), while there was no significant difference in other morphological features between the two groups. In malignant potential features, there were significantly more patients with absolute washout <60% in malignancy group (n=14, 87.5%) compared to adenoma group (n=12, 52.2%; $p$=0.021). The relative washout <40% was also more frequent in malignancy group (n=16, 100%) compared to adenoma group (n=10, 43.5%, $p$<0.001).

**Table 3.** Comparison of computed tomography characteristics between malignancy group and adenoma group in patients who underwent adrenalectomy

| | Malignancy (n=23) | Adenoma (n=32) | *p*-value |
|---|---|---|---|
| Tumor size, cm (mean±SD) | 3.79 (±2.36) | 3.05 (±1.00) | 0.645 |
| Morphological features (%) | | | |
| Calcification | 1 (4.3) | 3 (9.4) | 0.632 |
| Heterogenous enhancement | 4 (17.4) | 8 (25) | 0.500 |
| Fat containing | 0 (0) | 2 (6.3) | 0.504 |
| Overall cystic | 1 (4.3) | 0 (0) | 0.426 |
| Internal cystic portion | 0 (0) | 0 (0) | |
| Irregular border | 7 (30.4) | 1 (3.1) | 0.007 |
| Malignant potential features (%) | | | |
| Tumor size ≥4 cm | 7 (30.4) | 6 (18.8) | 0.314 |
| Pre-contrast ≥10 HU | 18 (100) | 19 (79.2) | 0.060 |
| Absolute washout <60% | 14 (87.5) | 12 (52.2) | 0.021 |
| Relative washout <40% | 16 (100) | 10 (43.5) | <0.001 |

Additionally, we evaluated the 'selected malignancy-related features' including irregular border, absolute washout <60% and relative washout <40% to determine an appropriate treatment decision for patients with nonfunctioning adrenal incidentaloma (Table 4). All the patients with available data in malignancy group (n=20) presented three selected malignant-related features of CT scan whereas only 56.5% in adenoma group had these features ($p$<0.001).

**Table 4.** Comparison of patients with selected malignancy-related features between malignancy and adenoma in surgery group.

| Selected malignancy-related features (%) | Malignancy (n=20) | Adenoma (n=23) | *p*-value |
|---|---|---|---|
| Yes | 20 (100) | 13 (56.5) | <0.001 |
| No | 0 (0) | 10 (43.5) | |

**Discussion**

To evaluate the clinical manifestation of nonfunctioning adrenal incidentaloma, we analyzed 307 patients who underwent surgery or regular follow-up without surgical treatment. In this study we focused on the findings on CT scan since most of adrenal incidentaloma were detected by CT scan. Surgery group presented higher rate of malignant potential features on CT findings compared to observation group. The mean tumor size of surgery group was ≥4 cm which was larger than the observation group, a renowned criterion of size that recommends surgery [18]. However, the mean tumor size of malignancy group within the patients who underwent adrenalectomy was less than 4 cm, which opposes the malignant size criteria of adrenal tumor findings.

Regarding reason of performing CT, it is interesting that subjects who did CT as a work-up for malignancies possessed higher portion in observation group (n=58, 32.2%). This follows previous study that over half of adrenal incidentalomas detected in patients with contemporary malignancy were benign [8]. CT features consistent with malignancy were significant in surgery group, and the majority of morphological features related to malignant potential was more prominent in surgery group when compared to observation group. This could suggest that the patients in surgery group were the eligible candidates to receive surgical treatment because they possessed significant CT features that suggests malignancy.

Moreover, according to final pathologic results in surgery group, diverse diagnoses other than adrenal cortical adenoma were confirmed. Previous studies have shown that incidentally detected adrenal incidentalomas are mostly nonfunctioning benign mass, some are functional with small number of malignancies [1, 19]. However, our data shows that benign adenoma was only 25%, while malignancy occupied 18% of surgically-resected adrenal incidentaloma. This means that when we encounter nonfunctioning adrenal incidentaloma, we should not limit its entity to benign tumor. This also justifies surgical treatment of nonfunctioning adrenal incidentaloma in certain circumstances for pathologic confirm and proper management.

For further explanation, we performed additional analysis between two subgroups of the surgery group: malignancy and adenoma group. Interestingly, both groups had the mean tumor size on CT scan less than 4 cm, which does not fulfill the size criteria for surgery. This follows results of previous Korean studies that suggested size criteria less than 4 cm should also be considered as surgical indication [19, 20]. Also, this means that a nonfunctioning adrenal tumor should be suspected for malignancy in certain circumstances even if its size is smaller than 4 cm.

Although a previous study questioned the power of washout value to characterize adrenal incidentalomas [21], washout measurement could be suggested as an effective tool to decide surgical resection. According to our study result, it expected pathologic result of a malignant tumor. Our finding suggests that when an adrenal incidentaloma is detected, contrast-enhanced CT has its own role for further identification of the tumor.

Among CT findings, irregular border, absolute washout <60% and relative washout <40% were significant factors regarding malignancy in our study group among the surgery group, and we described them as selected malignancy-related features. Since tumor size 4 cm or larger was not correlated with adrenal malignancy in this study, these three selected malignancy-related features were more practical prognosis-predictive factors that relate to malignant pathologic result of a nonfunctioning adrenal incidentaloma. This means that nonfunctioning adrenal incidentalomas should be considered for surgical resection if they possess suggested CT features, even though the size is smaller than 4 cm.

Not only malignant adrenal incidentalomas are surgical candidates, but also patients with other diseases can benefit from adrenalectomy. Lei et al. explained that adrenal ganglioneuroma is indicated for surgical resection because it can cause abdominal discomfort and show malignant transformation [22]. Also, patients with adrenal myelolipoma can benefit from surgery if they have abdominal or flank pain due to the nature of growing to large size [23]. There has been reports about pathologically-proven pheochromocytomas with normal hormone level. These so-called silent pheochromocytomas have clinical significance to get resected because of their possible complications [24]. This means that surgical resection of adrenal incidentaloma offers clinical advantages to certain group of patients with non-malignant adrenal diseases.

Our study has following limitations. Retrospective nature of the study may have allowed selection bias regarding physician's decision to refer for surgery. Therefore, larger number of patients in multi-center setting is required for more precise analysis. Nevertheless, previous studies on adrenal incidentalomas have mainly focused on risk factors about functioning adenomas or have small number of patients that have undergone surgery. Therefore, our study has strength that we enrolled patients with nonfunctioning adrenal incidentalomas, divided them into surgery and observation group, compared two groups regarding clinical characteristics and CT findings in a long-term basis, and most importantly, figured out factors that lead to decision of surgical management and suggest malignancy.

**Conclusion**

When a nonfunctioning adrenal incidentaloma is encountered, it is important to decide the appropriate treatment direction to yield favorable prognosis. For such determination, CT findings of malignant potential features seem highly associated with detecting malignancy after diagnostic adrenalectomy. Moreover, irregular borders, absolute washout value less than 60% and relative washout value less than 40% were significantly related to malignant pathologic results. However, the size of adrenal tumor 4 cm or larger was not associated with malignant adrenal disease in this study, which suggests that the size criteria is not reliable on its own. Patients with adrenal tumor smaller than 4 cm should be considered for surgical resection if the tumor has at least one of three selected malignancy-related features mentioned earlier, because they seem as more effective predictors to detect malignancy.

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## 국문요약

부신 우연종은 부신질환 이외 질병에 대한 검사에서 발견되는 부신 종양으로, 대개 비기능성이고 양성으로 알려져 있다. 전산화단층촬영 (CT) 영상이 진단 및 감별에 도움이 되며, 기능성이거나 악성인 경우 수술적 절제의 대상이 된다. 비기능성 부신 우연종은 주로 경과관찰의 대상이지만, 특정 환자군에서 적절한 치료를 위해 부신 절제술을 필요로 하는 경우가 있다. 본 연구의 목적은 비기능성 부신 우연종 환자에서 적합한 치료 방향을 결정하는데 관련 있는 예후 인자를 알아보는 데 있다.

본 연구는 단일기관 후향적 연구로, 2000년 1월부터 2020년 12월까지 서울아산병원 내분비외과, 내분비내과를 내원하여 비기능성 부신 우연종을 진단받은 환자들을 대상으로 하였다. 환자들을 수술군과 경과관찰군으로 나누고, 수술군 내에서 병리결과가 악성인 환자들과 양성 샘종인 환자들을 추가로 비교하였다. 기본 임상 정보와 혈액검사, CT 소견과 병리결과를 정리하였고, 특히 CT 소견 중 종양의 크기, 하운스필드 단위, 세척값과 같이 악성 부신종양과 관련 있는 값을 측정 및 계산하였다.

총 307명의 환자가 본 연구에 포함되었고, 수술군 환자 127명, 경과관찰군 환자 180명이었다. 수술군이 경과관찰군에 비해 평균 나이가 어리고, 평균 종양 크기가 큰 것으로 나타났다 ($p < 0.05$). 수술군에서 부신절제술 이유로 가장 많이 차지한 것은 종양 크기가 4cm 이상인 경우로 35.4%였고, 그 다음 25.2%의 환자에서 종양 크기의 증가로 인해 수술을 시행하였다. 경과관찰군에서는 50명 (28.8%)의 환자가 경과관찰 중 종양 크기의 증가를 보였다. CT 소견을 비교했을 때 수술군에서 경과관찰군보다 대부분의 형태적 특징, 모든 악성 종양 관련 특징이 더 높은 비율로 나타났으며, 수술군에서 병리결과를 분석했을 때 부신 샘종이 25%로 가장 많았고, 그 다음은 전이암 (14%)이었다.

수술군 내 추가분석에서 악성 종양군과 샘종군 모두 평균 크기는 4cm보다 작았고, 악성 종양군은 샘종군에 비해 종양이 불규칙한 경계를 가진 경우, 절대적 세척값이 60% 미만이거나 상대적 세척값이 40% 미만인 환자가 더 높은 비율로 나타났다.

결론적으로, 비기능성 부신 우연종은 항상 좋은 예후를 보이지 않으므로 감별진단을 거쳐 적절히 치료하는 것이 중요하다. 본 연구 결과 CT 소견 중 하운스필드 단위와 세척값과 같이 악성 종양과 관련 있는 특징들은 수술적 치료 결정에 도움이 되었다. 하지만, 기존에 제시된 수술적 치료 기준인 4cm 이상 크기는 악성 부신종양을 예측하는데 적합하지 않았다. 따라서 부신 우연종 환자에서 앞서 언급된 특징들을 보이는 경우, 비기능성이라고 경과관찰하기 보다는 적절한 치료를 위해 수술적 절제를 적극적으로 고려해야 한다.