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Clinicopathological Features of Ovarian Adult Granulosa Cell Tumor in Dr. Hasan Sadikin General Hospital Bandung from 2019 to 2025

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ABSTRACT

Adult granulosa cell tumor (AGCT) is the most common ovarian sex cord–stromal tumor (SCST), comprising approximately 70% of cases. This study aimed to describe the clinicopathological features of AGCT patients treated at Dr. Hasan Sadikin General Hospital, Bandung, from 2019 to 2025. This observational analytic study included 46 women who underwent surgical resection and were histopathologically diagnosed with AGCT, with documented International Federation of Gynecology and Obstetrics (FIGO) stage, at Dr. Hasan Sadikin General Hospital between 2019 and 2025. Sampling was consecutive. Variables observed included age, FIGO stage, laterality, ascites, surgical procedures, tumor size, histopathological pattern, mitotic count, necrosis, lymphovascular invasion, endometrial pathology, and adjuvant chemotherapy. Data were analyzed descriptively. The mean age of patients was 47 years (range: 19–63). The mean tumor size was 23.7 cm, and most tumors (82.6%) measured ≥10 cm. Nearly all were unilateral (97.8%), with a slight predominance in the right ovary (54.3%). Ascites was present in 56.5% of patients. Histologically, 89.1% exhibited multiple admixed growth patterns with low mitotic activity. Necrosis and lymphovascular invasion were observed in 30.4% and 17.4% of cases, respectively. Endometrial alterations were rare (6.5%). Stage distribution was 47.8% stage I, 2.2% stage II, 41.3% stage III, and 8.7% stage IV. Adjuvant chemotherapy was administered to 50% of patients, most frequently paclitaxel–carboplatin (60.8%). AGCTs in this cohort were predominantly large, unilateral tumors with admixed histological patterns and low mitotic activity. Necrosis and lymphovascular invasion occurred more often in advanced stages, indicating potential prognostic significance.

KEYWORDS *Clinicopathological, Adult Granulosa Cell Tumor, Bandung*

INTRODUCTION

Granulosa cell tumors (*GCT*) are a rare malignant subtype of ovarian tumors, Jung et al., (2023) accounting for 2–5% of all ovarian malignancies Şahin et al., (2024) and classified into adult and juvenile subtypes based on clinical and histopathological features (Li et al., 2022; Li et al., 2018). Approximately 95% of cases are adult granulosa cell tumors (*AGCT*), Li et al., (2018) which represent the most common ovarian sex cord–stromal tumor (*SCST*), comprising about 70% of cases (Gogola-Mruk et al., 2021; Plett et al., 2023). *AGCT* typically presents as a low-grade malignant neoplasm with a marked tendency for late recurrence and distant metastasis (Färkkilä et al., 2017). Although most *AGCTs* are diagnosed at an early stage, up to 50% of patients with relapsed disease may ultimately succumb to the tumor (Ding et al., 2019).

Previous studies have identified tumor stage and tumor rupture in stage I disease as the most important prognostic factors (Fashedemi et al., 2019). The 5-year disease-specific survival rates are 98%, 84%, 61%, and 41% for Stages I, II, III, and IV, respectively (Li et al., 2021). The National Comprehensive Cancer Network (*NCCN*) guidelines recommend adjuvant chemotherapy for stage II–IV *AGCT* after complete resection (Färkkilä et al., 2017).

Clinicopathological characteristics such as tumor size, necrosis, lymphovascular invasion, and associated endometrial pathology remain variably reported, and their prognostic

significance is not fully established. Data on *AGCT* from Indonesia are limited, and no prior study has comprehensively described its clinicopathological spectrum in the local population. This study aims to analyze the clinicopathological characteristics of *AGCT* patients treated at Dr. Hasan Sadikin General Hospital, Bandung, from 2019 to 2025, thereby providing insight into the heterogeneity of *AGCT* and its potential prognostic determinants in an Indonesian population.

Van Meurs et al. (2014) conducted a multicenter study involving European populations and identified tumor stage and rupture as the strongest predictors of recurrence and overall survival. However, their cohort lacked detailed analysis of histopathological variations such as lymphovascular invasion and endometrial pathology, which may influence tumor behavior. Meanwhile, Jamieson and Fuller (2020), in their population-based study, emphasized the indolent nature of *AGCT* and its prolonged risk of late recurrence, yet they noted that data from Asian populations are scarce, especially regarding how clinicopathological factors correlate with prognosis. Both studies underline a significant gap in regional data, particularly from Southeast Asia, where environmental, genetic, and healthcare factors may alter disease presentation and outcomes.

Building upon these gaps, the present study provides a comprehensive analysis of *AGCT* cases in Indonesia, focusing on clinicopathological characteristics, prognostic factors, and disease progression patterns in patients treated at Dr. Hasan Sadikin General Hospital, Bandung. The findings are expected to enrich global literature by contributing data from an underrepresented population and to serve as a reference for clinicians in improving diagnostic accuracy, prognostic evaluation, and personalized treatment strategies for *AGCT* in Indonesia and similar low-resource settings.

METHOD

This study was an observational analytic study with a retrospective design. The subjects were women who underwent surgical resection and were histopathologically diagnosed with adult granulosa cell tumor (AGCT) with documented International Federation of Gynecology and Obstetrics (FIGO) stage. The study was conducted at Dr. Hasan Sadikin General Hospital, Bandung, between January 2019 and March 2025.

The study population initially consisted of 51 patients. Five patients were excluded due to incomplete staging information, resulting in a final sample size of 46 patients. The median age at diagnosis was 47 years (range: 19–66 years). Data were obtained from hospital medical records and pathology archives. Variables analyzed included patient age, FIGO stage, tumor laterality, presence of ascites, surgical procedures, tumor size, histopathological growth pattern, mitotic index, necrosis, lymphovascular invasion, endometrial pathology, and administration of adjuvant chemotherapy.

Histopathological patterns were determined from paraffin-embedded tissue blocks prepared routinely and stained with hematoxylin and eosin (H&E). Mitotic activity was assessed per 10 high-power fields (HPF). The presence of necrosis, lymphovascular invasion, and endometrial changes was recorded according to standard morphological criteria (Jung et al., 2023). This study protocol was approved by the Health Research Ethics Committee of Padjadjaran University (No. 730/UN6.KEP/EC/2025).

RESULT AND DISCUSSION

A total of 46 women diagnosed with AGCT between 2019 and 2025 at Dr. Hasan Sadikin General Hospital were included in this analysis. The median age at diagnosis was 47 years (range, 19–63 years). The mean tumor size was 23.7 cm (range, 6–50 cm), with 82.6% (n = 38) of patients presenting with tumors ≥10 cm. Tumor size data were not available (NA) in 6.5% (n = 3) of cases due to prior surgery at other hospitals. Unilateral involvement was observed in 45 patients (97.8%), slightly more frequently in the right ovary (54.3%, n = 25). Ascites was identified in 56.5% (n = 26) of cases.

Regarding surgical management, 13 patients (28.3%) underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy and complete staging, which included peritoneal washings, peritoneal biopsies, appendectomy, and omental sampling with or without lymph node dissection.

Histopathological analysis revealed that most tumors (89.1%, n=41) displayed two or more admixed growth patterns, predominantly diffuse, insular, trabecular, and microfollicular. The mitotic index was uniformly low (<10/10 HPF) in all cases. Tumor necrosis was identified in 30.4% (n=14), while lymphovascular invasion was detected in 17.4% (n=7). Endometrial alterations were observed in 3 patients (6.5%), consisting of simple hyperplasia without atypia (n=2) and complex atypical hyperplasia (n=1).

The distribution of FIGO stages was as follows: stage I, 47.8% (n = 22); stage II, 2.2% (n = 1); stage III, 41.3% (n = 19); and stage IV, 8.7% (n = 4). Adjuvant chemotherapy was administered in 50% of patients (n = 23), most commonly with paclitaxel–carboplatin (60.8%, n = 14). Chemotherapy data were incomplete in 21.7% (n = 10) of cases because the information was not available in the medical records. The characteristics of the AGCT patients are summarized in Table 1.

Table 1. Clinicopathological characteristics of patients

Characteristics	Total (n=46)(%)
Age	
Median (year)	47
Range	19-63
≤ 50	29 (63)
> 50	17 (37)
FIGO stage	
I	22 (47.8)
II	1 (2.2)
III	19 (41.3)
IV	4 (8.7)
Laterality	
Left	20 (43.5)
Right	25 (54.3)
Bilateral	(2.2)
Ascites	
Absent	20 (43.5)
Present	26 (56.5)
Surgical procedure	
Complete	13 (28.3)
Incomplete	33 (71.7)
Tumor size	

Characteristics	Total (n=46)(%)
≤ 10 cm	5 (10.9)
> 10 cm	38 (82.6)
Not available	3 (6.5)
Histopathological pattern	
Mixed pattern	41 (89.1)
Single pattern	5 (10.9)
Mitosis	
≤ 10/10 HPF	46 (100)
> 10/10 HPF	0 (0)
Necrosis	
Absent	32 (69.6)
Present	14 (30.4)
Lymphovascular invasion	
Absent	39 (82.6)
Present	7 (17.4)
Endometrial pathology	
None	43 (93.5)
Hyperplasia without atypia	2 (4.3)
Hyperplasia with atypia	1 (2.2)
Carcinoma	0 (0)
Adjuvant chemoterapy	
No	13 (28.3)
Yes	23 (50)
NA	10 (21.7)

There were no significant differences in age, presence of ascites, histopathological growth pattern, mitotic index, or endometrial pathology between stages. However, tumor necrosis and lymphovascular invasion were more frequent in advanced-stage disease. A summary of clinicopathological characteristics according to FIGO stage is presented in Table 2.

Table 2. Comparison between characteristics patients with FIGO stage

Characteristics	FIGO stage			
	FIGO I (n=22)(%)	FIGO II (n=1)(%)	FIGO III (n=19)(%)	FIGO IV (n=4)(%)
Age				
≤ 50	16 (72.7)	0 (0)	10 (52.6)	3 (75)
> 50	6 (27.3)	1 (100)	9 (47.4)	1 (25)
Ascites				
Absent	8 (36.4)	0 (0)	9 (47.4)	4 (100)
Present	14 (63.6)	1 (100)	11 (52.6)	0 (0)
Tumor size				
≤ 10	1 (4.5)	1 (100)	2 (10.5)	0 (0)
> 10	21 (95.5)	0 (0)	17 (89.5)	4 (100)
NA	0 (0)	0 (0)	0 (0)	0 (0)
Histopathological pattern				
Mixed pattern	18 (81.8)	1 (100)	19 (100)	3 (75)
Single pattern	4 (18.2)	0 (0)	0 (0)	1 (25)
Mitosis				
≤ 10/10 HPF	22 (100)	1 (100)	19 (100)	4 (100)
> 10/10 HPF	0 (0)	0 (0)	0 (0)	0 (0)
Necrosis				
Absent	20 (90.9)	1 (100)	11 (57.9)	2 (50)
Present	2 (9.1)	0 (0)	8 (42.1)	2 (50)
Lymphovascular invasion				

Characteristics	FIGO stage			
	FIGO I (n=22)(%)	FIGO II (n=1)(%)	FIGO III (n=19)(%)	FIGO IV (n=4)(%)
Absent	20 (90.9)	0 (0)	15 (78.9)	3 (75)
Present	2 (9.1)	1 (100)	4 (21.1)	1 (25)
Endometrial pathology				
None	21 (95.5)	1 (100)	17 (89.4)	4 (100)
Hyperplasia without atypia	1 (4.5)	0 (0)	1 (5.3)	0 (0)
Hyperplasia with atypia	0 (0)	0 (0)	1 (5.3)	0 (0)
Carcinoma	0 (0)	0 (0)	0 (0)	0 (0)

Discussion

AGCT is the most common subtype of ovarian sex cord-stromal tumors (SCST), accounting for approximately 70% of cases (Gogola-Mruk et al., 2021; Plett et al., 2023). The mean age at diagnosis is around 50 years, with 57% of patients reported between 30–60 years and 12% younger than 30 years (Li et al., 2018; Sakr et al., 2017). In our study, 37% of patients were diagnosed at age >50 years, with an overall age range of 19–63 years. This finding is largely consistent with previous reports, although the proportion of patients older than 50 years in our study was relatively lower. These results suggest that while AGCT typically presents in middle-aged women, it can also occur in younger patients, underscoring the importance of considering this diagnosis across a wider age spectrum.

Complete staging surgery is emphasized in some published reports although the role of lymphadenectomy is highly controversial and the majority of published papers did not support the routine use of lymphadenectomy during complete staging surgery, based on the extremely low incidence of lymph node metastases in patients with GCT (Huang et al., 2014; Betit et al., 2025). In our study, 28.3% of patients underwent complete staging surgery, including total abdominal hysterectomy with bilateral salpingo-oophorectomy. The relatively low proportion of patients who underwent full staging in our study may reflect the prevailing consensus that lymph node dissection provides limited prognostic or therapeutic value in AGCT.

Ascites is very rarely seen in patients with AGCT (Färkkilä et al., 2017). Interestingly, in our study more than half of the patients (56.5%) presented with ascites, a markedly higher proportion compared with previous reports. This discrepancy may reflect differences in patient population, tumor stage at diagnosis in our institution.

Macroscopically, AGCT usually unilateral and large, with reported sizes ranging from 3 cm to 24 cm and a mean diameter of approximately 10 cm Esther & Joseph, 2020; Rosai, 2011; Chou & Huang, 2016). In the present study, AGCTs demonstrated a wide size range, from 6 cm up to 50 cm, with a mean diameter of 23.7 cm. Notably, the majority of cases (82.6%) measured ≥10 cm, which is considerably larger than the average size reported in the literature. This discrepancy may reflect a delay in clinical detection. Unilateral involvement was observed in most patients (95.7%), with a slight predominance in the right ovary (54.3%). This is in line with literature reporting unilateral disease in the vast majority of cases, although the side predilection is not consistently described. The relatively high frequency of large tumors in our series underscores the importance of considering AGCT in the differential diagnosis of unilateral ovarian masses, particularly those exceeding 10 cm in diameter (Li et al., 2018; Li et al., 2021; Li et al., 2022).

Microscopically, AGCTs may display a wide variety of architectural patterns, often occurring in combination within the same tumor. The most common pattern is diffuse, but tumor cells may also be arranged in cords or trabeculae, form insular nests resembling islands of varying size, or adopt a microfollicular pattern characterized by Call-Exner bodies-small spaces filled with eosinophilic or hyalinized material surrounded by granulosa cells. Less frequently observed patterns include gyriform, watered silk, macrofollicular, sarcomatoid, and pseudopapillary arrangements (Yang & Stack, 2020; Babarović et al., 2018).

The tumor cells typically exhibit uniform, pale, round to oval nuclei with irregular nuclear membranes and characteristic nuclear grooves, accompanied by scant cytoplasm. Mitotic activity is generally low (Esther & Joseph, 2020). The diffuse and insular patterns were the most frequently encountered in our study, in line with earlier observations describing these as predominant in AGCT. Microfollicular structures with Call-Exner bodies, although not always present, remain a useful diagnostic clue due to their relative specificity. Less frequent patterns, such as gyriform, watered silk, macrofollicular, sarcomatoid, and pseudopapillary, were reported in the literature but were not commonly observed in our study. Mitotic activity was uniformly low (<10/10 HPF) in all of our cases, consistent with literature. Of note, necrosis was identified in nearly one-third of cases (30.4%), a finding that has been variably reported in prior studies. Lymphovascular invasion, observed in 17.4% of our tumors, may represent an adverse prognostic feature, although its significance in AGCT remains uncertain due to limited and conflicting evidence in the literature.

AGCT may also lead to the development of endometrial carcinoma as a result of unopposed estrogen stimulation of the endometrium. An enlarged uterus with a thickened endometrium is often noted due to an estrogenic effect. Endometrial sampling may detect endometrial hyperplasia in 25-50% of patients with AGCT and endometrial carcinoma in another 5-10%. In our series, 6.5% of patients had endometrial pathology, consisting of hyperplasia without atypia (4.3%) and complex hyperplasia with atypia (2.2%). Although the frequency observed in our study was relatively low compared to previous reports, these findings emphasize the importance of routine endometrial evaluation in AGCT patients, particularly in those presenting with abnormal uterine bleeding (Färkkilä et al., 2017).

The staging of AGCT is determined according to the International Federation of Gynecology and Obstetrics (FIGO) system (Färkkilä et al., 2017; Esther & Joseph, 2020). AGCTs most commonly present at stage I, typically confined to a unilateral ovary (Fashedemi et al., 2019). Tumor stage and the presence of tumor rupture in stage I disease have been identified as the most important prognostic factors (Ding et al., 2019). In contrast, a relatively high proportion of advanced-stage disease was observed in our series, with 41.3% of patients diagnosed at stage III and 8.7% at stage IV. Only 47.8% of patients presented with stage I disease, which is lower than expected based on previously published studys. This discrepancy may reflect delays in diagnosis, or biological variation in disease behavior within our population.

Tumor stage remains the single most important prognostic factor in AGCT, and even within stage I disease, the presence of tumor rupture has been shown to adversely impact outcome (Fashedemi et al., 2019). The higher frequency of advanced stages in our study underscores the need for heightened clinical suspicion and early detection strategies in patients

presenting with large unilateral ovarian masses. Moreover, these findings emphasize the prognostic significance of accurate staging in AGCT and its central role in guiding clinical management and follow-up.

According to the National Comprehensive Cancer Network (NCCN) guidelines, adjuvant chemotherapy is recommended for patients with completely resected AGCT at stages II to IV (Färkkilä et al., 2017). In early stage AGCT, only high risk patients (large tumors, tumors with high mitotic index, or ruptured tumors) should receive adjuvant chemotherapy (Kryvenko, 2022; Zhang et al., 2025). In our study, 50% of patients received adjuvant therapy, reflecting the relatively high proportion of advanced-stage disease. The most commonly used regimen was paclitaxel–carboplatin (60.8%), followed by bleomycin–etoposide–cisplatin (34.9%), and cisplatin–vinblastine–bleomycin (4.3%).

The limitations of this study include its retrospective single-center design, modest sample size, and incomplete long-term follow-up, precluding definitive survival analysis. Future multicenter prospective studies with molecular profiling may clarify the prognostic significance of necrosis, lymphovascular invasion, and other pathological features.

CONCLUSION

This study, conducted at Dr. Hasan Sadikin General Hospital, Bandung (2019–2025), highlights the biological heterogeneity of AGCT, characterized by predominantly large tumors, mixed histopathological growth patterns, and consistently low mitotic activity across all FIGO stages. Necrosis and lymphovascular invasion were more prevalent in advanced stages, suggesting their significance in disease progression, while endometrial alterations, though rare, underscore the need for routine endometrial evaluation. These results reaffirm the prognostic importance of stage, necrosis, and lymphovascular invasion, and future research should explore the molecular and genetic underpinnings of these clinicopathological factors to better predict outcomes and guide personalized treatment strategies in AGCT.

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