AEG-1 expression analysis in epithelial ovarian carcinoma: Uncovering distinctions between high-grade and low-grade serous carcinoma

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Received January 17, 2025; Accepted May 22, 2025

DOI: 10.3892/mco.2025.2865

Abstract. Epithelial ovarian carcinoma (EOC) is the most common form of ovarian cancer and is associated with a poor prognosis. Astrocyte Elevated Gene-1 (AEG-1) is an oncogene implicated in cancer cell growth and progression. The present study examined AEG-1 expression in EOC, specifically comparing high-grade serous ovarian carcinoma (HGSOC) and low-grade serous ovarian carcinoma (LGSOC). The present retrospective analytical study employed a cross-sectional design and included women diagnosed with HGSOC or LGSOC between January 2021 and December 2023. Extracted data included demographic, laboratory and clinicopathological characteristics. In addition to comparing AEG-1 expression in HGSOC and LGSOC, associations between these histological subtypes and the extracted variables, as well as associations between AEG-1 expression and these variables, were assessed. Of the 74 patients initially identified, 24 were excluded, resulting in a final sample of 50 patients 23 with LGSOC and 27 with HGSOC. A statistically significant association was found between residual disease and cancer histopathology [odds ratio: 7.219; 95% confidence interval (CI): 1.399-37.252; P=0.024), whereas no significant associations were observed with other variables. AEG-1 expression was significantly higher in HGSOC compared with LGSOC (relative risk: 3.228; 95% CI: 1.188-8.776; P=0.012), with high AEG-1 expression observed more frequently in HGSOC (65.7%) than in LGSOC (34.3%). In conclusion, AEG-1 expression was significantly elevated in HGSOC compared with LGSOC, suggesting a potential role for AEG-1 in the progression of HGSOC.

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Key words: ovarian cancer, epithelial ovarian carcinoma, high-grade serous carcinoma, low-grade serous carcinoma, astrocyte elevated gene-1, metadherin

Introduction

Ovarian cancer (OC) remains a critical public health concern due to its poor prognosis and high mortality rate (1,2). According to 2022 GLOBOCAN data, OC is the eighth most common cancer and the eighth leading cause of cancer-related death among women worldwide, accounting for 206,956 deaths (3). This high mortality may be attributed to the lack of symptoms in early-stage disease and the absence of effective screening methods (4,5). Consequently, OC is frequently diagnosed at an advanced stage, contributing to its poor prognosis (6,7). Additionally, the disease is marked by a high recurrence rate, with over 80% of cases developing resistance to treatment, leading to a reduced 5-year survival rate (8).

Epithelial ovarian carcinoma (EOC) is the most common subtype of OC, comprising ~90% of all ovarian malignancies (4,9). EOCs are classified into Type I and II based on their histopathological features and clinical behavior (10-12). Low-grade serous ovarian carcinoma (LGSOC), a Type I tumor, is typically indolent, associated with prolonged overall survival, and presents a relatively favorable prognosis (11,13,14). It is often linked to serous borderline tumors, which are considered common precursor lesions (15,16). LGSOC is frequently associated with mutations in the MAPK signaling pathway, particularly involving the KRAS and BRAF genes (17,18). By contrast, high-grade serous ovarian carcinoma (HGSOC) is a Type II tumor characterized by aggressive growth, rapid progression, and poor clinical outcomes. It is frequently diagnosed at an advanced stage (10,11,19,20). Serous tubal intraepithelial carcinoma, arising from the distal fimbriae of the fallopian tube, has been identified as a probable precursor lesion of HGSOC (21-23). Genomic analyses have revealed

that ~96% of HGSOC cases harbor mutations in the TP53 gene (24-27).

Astrocyte Elevated Gene-1 (AEG-1), also known as metadherin, is an oncogene that plays a crucial role in cancer development and progression (28,29). AEG-1 interacts with various proteins and activates key oncogenic signaling pathways, including NF-κB, PI3K/Akt, MEK/ERK and Wnt/β-catenin (28,30). This activation promotes multiple cancer hallmarks, such as increased proliferation, migration, invasion, angiogenesis and metastasis (30-32). Furthermore, AEG-1 expression has been associated with chemotherapy resistance in several cancer types, including OC (33,34). It has been previously shown that elevated AEG-1 expression in EOC correlates with clinicopathological features such as disease stage, tumor grade, residual tumor size, lymph node metastasis and poor prognosis (30).

HGSOC and LGSOC differ in their clinical characteristics and prognoses (14). They also exhibit distinct responses to chemotherapy (19). As such, understanding the molecular differences between these two subtypes of EOC is essential for guiding appropriate treatment strategies. Given AEG-1's involvement in cancer progression and its potential influence on chemotherapy response (28,34), further investigation is warranted. However, the specific role of AEG-1 in EOC, particularly in HGSOC and LGSOC, remains unclear. Therefore, the present study aimed to examine differences in AEG-1 expression between HGSOC and LGSOC and to determine whether AEG-1 expression can be used to distinguish between these two subtypes.

Materials and methods

Study design and data source. The current retrospective analytical study employed a cross-sectional design. The research was conducted at the Division of Gynecological Oncology, Department of Obstetrics and Gynecology, and the Department of Anatomical Pathology, Faculty of Medicine (Airlangga University, Dr Soetomo Hospital, Surabaya, Indonesia). Data were obtained from electronic medical records that were collected between May 2024 and September 2024. The study population consisted of women diagnosed with HGSOC or LGSOC who underwent surgical treatment at Dr Soetomo Hospital between January 2021 and December 2023. All diagnoses were confirmed through histopathological examination.

The inclusion criteria were as follows: i) complete medical record data; ii) patients who underwent surgical procedures at Dr Soetomo Hospital, Surabaya; iii) histopathological confirmation of either low-grade or HGSOC; and iv) availability of paraffin blocks stored at the Anatomical Pathology Laboratory of Dr Soetomo Hospital during the study period (2021 to 2023). Patients who had received neoadjuvant chemotherapy (NAC) or whose histopathological results originated from institutions other than Dr. Soetomo Hospital were excluded.

Primary data were obtained from the medical records of patients meeting the inclusion and exclusion criteria. The study materials consisted of paraffin-embedded tumor mass tissue blocks obtained from surgical procedures conducted at Dr Soetomo Hospital. Immunohistochemical analysis was performed using an AEG-1 antibody (cat. no. 517220; Santa Cruz Biotechnology, Inc.). Deparaffination was performed by immersion in xylene and rehydration was achieved using a descending ethanol series (96, 90 and 80%). To prevent endogenous peroxidase activity, 3% H_2O_2 in methanol was used at room temperature (RT) for 15 min. The tissue blocks were incubated with AEG-1 antibody at 4˚C overnight, then stained with DAB at RT for 5 min and finally counterstained with Meyer's haematoxylin at RT for 5-10 min.

Data extraction and synthesis. The extracted data included demographic, laboratory and clinicopathological characteristics. Demographic variables comprised age, parity, age at menarche and menopausal status. The laboratory variable assessed was the serum CA 125 level. Clinicopathological factors included the presence of residual tumors and cancer stage. The present study evaluated key factors associated with HGSOC, LGSOC and AEG-1 expression.

The primary objective was to compare AEG-1 expression between HGSOC and LGSOC. Additionally, associations between the extracted variables and the histopathological subtypes (HGSOC and LGSOC), as well as the relationship between these variables and AEG-1 expression, were analyzed.

Expression level of AEG-1. AEG-1 expression levels were classified using a semiquantitative method based on the proportion of tumor cells exhibiting positive staining and the intensity of that staining. The proportion of positive cells was scored as follows: 0, no positive cells; 1, <10%; 2, 10-50%; and 3, >50%. Staining intensity was scored as: 0, no staining; 1, weak; 2, moderate; and 3, strong. The total AEG-1 expression score was calculated by summing the proportion and intensity scores. A total score of 4 or higher was considered high AEG-1 expression, while a score of 3 or lower was considered low AEG-1 expression (35,36).

Statistical analysis. Statistical analysis was performed using IBM SPSS Statistic version 29.0.0.0 (IBM Corp.). The primary statistical analysis of the collected data was conducted using the Mann-Whitney test to assess differences in AEG-1 expression between HGSOC and LGSOC. In addition, the chi-square test or Fisher's exact test were used to evaluate the relationships between clinical and demographic characteristics across the two groups. $P<0.05$ was considered to indicate a statistically significant difference.

Results

A total of 74 patients were diagnosed with either HGSOC or LGSOC. Of these, 24 patients met the exclusion criteria, including 13 patients for whom no paraffin blocks were available, six patients whose paraffin blocks contained no identifiable tumor cells, four patients who had received NAC, and one patient with incomplete data. Based on the inclusion and exclusion criteria, a final sample of 50 patients was included in the study. The cohort consisted of 27 patients with HGSOC and 23 with LGSOC (Fig. 1).

AEG-1 expression was evaluated by immunohistochemistry. AEG-1 was predominantly localized in the cytoplasm, nuclear membrane, or cell junctions. Staining was assessed across 10 randomly selected high-power fields (magnification, x400) representative of the average tumor size (Fig. 2).

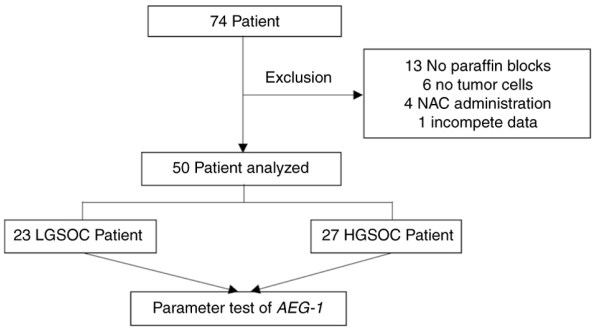

Figure 1. Schematic representation of research subject selection. HGSOC, high-grade serous ovarian carcinoma; LGSOC, low-grade serous ovarian carcinoma; NAC, neoadjuvant chemotherapy.

Characteristics of research subjects. Among the 50 participants, 34 (68%) were under 55 years of age, and 16 (32%) were over 55. A total of 19 patients (38%) were nulliparous, while 21 (42%) were multiparous. Early menarche (age, <12 years) was reported in 26 participants (52%), whereas 24 (48%) experienced menarche at age >12 years. Menopausal status was evenly distributed, with 25 patients (50.0%) post-menopausal and 25 (50%) pre-menopausal. Normal CA 125 levels were observed in 5 samples (10%), while elevated levels (>35 ng/ml) were identified in 45 samples (90%). Residual tumor size <1 cm was found in 37 patients (74%), and >1 cm in 13 patients (26%). Early-stage disease (FIGO stages I and II) was diagnosed in 25 patients (50%), and advanced-stage disease (stages III and IV) in the remaining 25 (50%). AEG-1 expression was low in 15 samples (30%) and high in 35 samples (70%). Regarding histological subtype, 23 cases (46%) were classified as LGSOC and 27 (54%) as HGSOC (Table I).

Table I. Descriptive distribution of patient data.

Patient characteristics	n (%)
Age, years	
≤55	34 (68)
>55	16 (32)
Parity	
Nullipara	19 (38)
Primipara	10 (20)
Multipara	21 (42)
Menarche	
Early menarche	26 (52)
Normal menarche	24 (48)
Menopausal status	
No	25 (50)
Yes	25 (50)
CA 125 level	
Normal	5 (10)
High	45 (90)
Residual tumor	
≤1 cm	37 (74)
>1 cm	13 (26)
Stage	
Early stage	25 (50)
Advanced stage	25 (50)
AEG-1 expression	
Low	15 (30)
High	35 (70)
Ovarian cancer	
Low grade	23 (46)
High grade	27 (54)

Relationship between the characteristics of research subjects and OC. The characteristics associated with OC incidence were analyzed to determine whether age, parity, menarche, menopausal status, CA 125 levels, residual tumor and cancer stage were related to LGSOC or HGSOC (Table II).

As shown in Table II, patients aged ≤55 years were slightly more common in the LGSOC group (69.6%) compared with the HGSOC group (66.7%). Nulliparous and primiparous women were more frequently observed in the HGSOC group (44.4 and 22.2%, respectively) than in the LGSOC group (30.4 and 17.4%, respectively). By contrast, multiparous women were more prevalent in the LGSOC group (52.2%) compared with the HGSOC group (33.3%). Early menarche (age, <12 years) occurred more often in patients with LGSOC (60.9%) than in those with HGSOC (44.4%). Among post-menopausal women, HGSOC was more prevalent (55.6%) than LGSOC (43.5%). Elevated CA 125 levels were observed in all patients with LGSOC (100%) and in 81.5% of those with HGSOC. Advanced-stage disease was more frequently found in HGSOC (51.9%) than in LGSOC (47.8%). Tumor residuals >1 cm were more commonly observed in HGSOC (40.7%) compared with LGSOC (8.7%).

According to the statistical analysis, only the variable related to residual tumor size yielded a P-value <0.05 (P=0.024), with an odds ratio (OR) of 7.219 [95% confidence interval (CI): 1.399-37.252], indicating a statistically significant association. The P-values and ORs for the other variables were as follows: age, P=1.000, OR=1.143 (95% CI: 0.346-3.777); parity, P=0.399; menarche, P=0.382, OR=1.944 (95% CI: 0.628-6.021); menopausal status, P=0.570, OR=1.625 (95% CI: 0.530-4.984); CA 125 level, P=0.540; and stage, P=1.000, OR =1.175 (95% CI: 0.386-3.576). These results suggest that no statistically significant associations were found between histological subtype (HGSOC or LGSOC) and the variables of age, parity, menarche, menopausal status, CA 125 level, or cancer stage.

Relationship between the characteristics of research subjects and AEG-1 expression. The association between AEG-1 expression and various clinical and demographic characteristics including age, parity, menarche, menopausal status, CA 125 level, residual tumor presence and cancer stage-was analyzed to explore potential relationships with low and high AEG-1 expression (Table III).

According to Table III, patients aged ≤55 years had a higher prevalence of high AEG-1 expression (74.3%) compared with those with low AEG-1 expression (53.3%). Nulliparous and multiparous women showed a greater prevalence of low

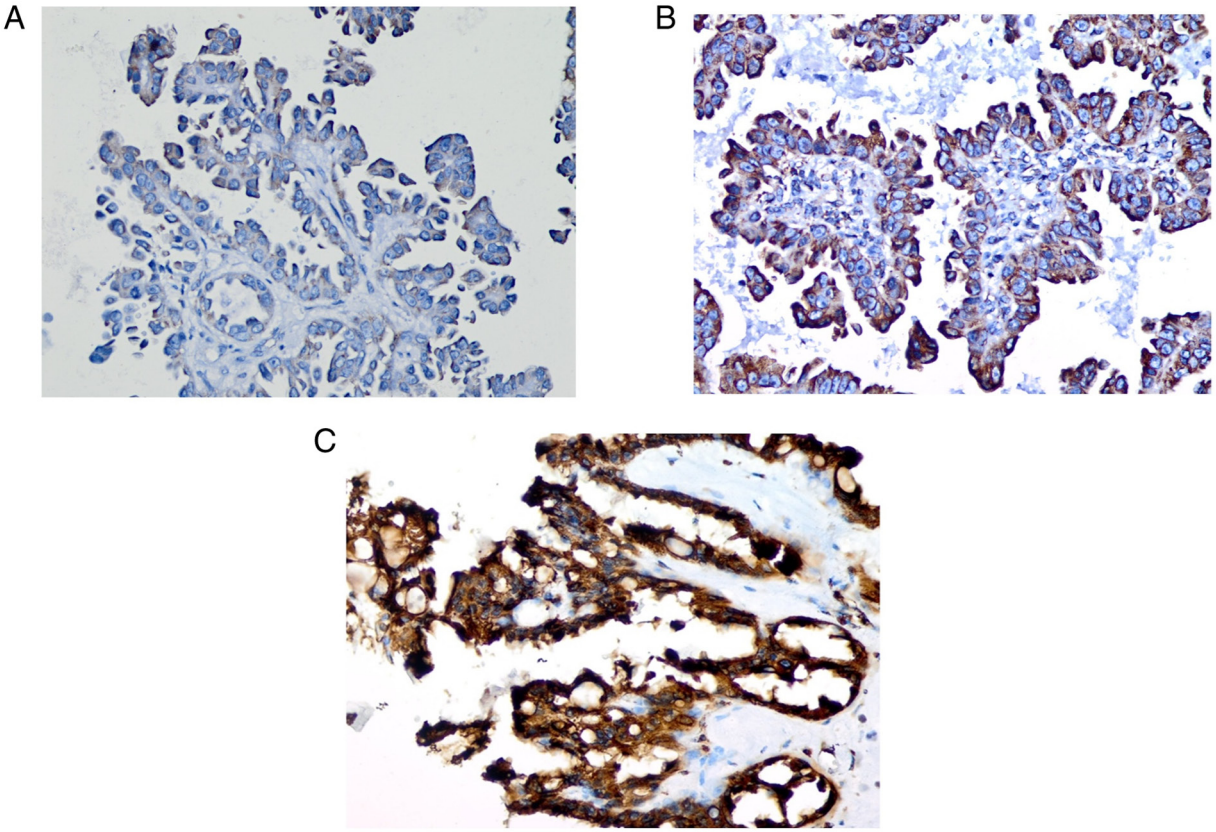

Figure 2. Expression of Astrocyte Elevated Gene-1 (magnification, x400). (A) Proportion <50%, low staining. (B) Proportion >50%, moderate staining. (C) Proportion >50%, strong staining.

AEG-1 expression (40.0 and 53.3%, respectively) than high AEG-1 expression, which was observed in 37.1% of patients in both groups. By contrast, primiparous women exhibited a higher prevalence of high AEG-1 expression (25.7%) compared with low AEG-1 expression (6.7%). Early menarche (age, <12 years) was more frequent among individuals with low AEG-1 expression (73.3%) than among those with high expression (42.9%). Among pre-menopausal patients, a higher prevalence of high AEG-1 expression was observed (51.4%) compared with low expression (46.7%). Elevated CA 125 levels were more common among patients with low AEG-1 expression (100.0%) than those with high expression (85.7%). Advanced-stage disease was slightly more associated with high AEG-1 expression (54.3%) than low expression (40.0%). Residual tumors >1 cm were slightly more common in patients with low AEG-1 expression (26.7%) compared with those with high AEG-1 expression (25.7%).

The P-values for each variable were as follows: age, P=0.191, OR=0.396 (95% CI: 0.112-1.403); parity, P=0.275; menarche, P=0.095, OR=3.667 (95% CI: 0.974-13.806); menopausal status, P=1.000, OR=0.826 (95% CI: 0.246-2.776); CA 125 level, P=0.305; residual tumor, P=1.000, OR=0.952 (95% CI: 0.241-3.756); and stage, P=0.537, OR=1.781 (95% CI: 0.521-6.085). Since all P-values exceeded the threshold of 0.05, none of the assessed characteristics revealed a statistically significant association with AEG-1 expression.

Differential expression of AEG-1 in OC. AEG-1 expression was analysed to determine whether there was a significant difference between patients with LGSOC and those with HGSOC. The comparison was conducted using the Mann-Whitney U test (Table IV).

Among the 23 LGSOC samples, low AEG-1 expression was identified in 11 samples (73.3%), while high AEG-1 expression was observed in 12 samples (34.3%). By contrast, among the 27 HGSOC samples, low AEG-1 expression was found in four samples (26.7%), whereas high AEG-1 expression was detected in 23 samples (65.7%). Statistical analysis yielded a relative risk (RR) of 3.228, with a 95% CI of 1.188-8.776) and P=0.012.

Discussion

LGSOC and HGSOC are distinct tumor types with differing morphological features, pathogenesis and molecular profiles (17). LGSOC generally has a more favorable prognosis than HGSOC (11,37). In the present study, the initial cohort included 74 patients diagnosed with either HGSOC or LGSOC, comprising 45 patients with HGSOC and 29 with LGSOC. This distribution aligns with existing literature indicating that HGSOC is more prevalent than LGSOC (13,38). HGSOC is the most common subtype of EOC, accounting for ~2/3 of cases and representing ~70% of the total incidence (21,39). By contrast, LGSOC comprises ~5% to 10% of all serous ovarian carcinoma cases (40,41).

The present study investigated several demographic characteristics, including age, parity, menarche and menopausal status. While research exploring the relationship between these variables and AEG-1 expression is limited, numerous

Table II. Characteristic evaluation for ovarian cancer.

Patient characteristics	Total (n=50)	Ovarian cancer		Raw P-value	Adjusted P-value
		Low grade, n (%)	High grade, n (%)		
Age, years					
≤55	34	16 (69.6)	18 (66.7)	1.000	1.167
>55	16	7 (30.4)	9 (33.3)		
Parity					
Nullipara	19	7 (30.4)	12 (44.4)	0.399	0.698
Primipara	10	4 (17.4)	6 (22.2)		
Multipara	21	12 (52.2)	9 (33.3)		
Menarche					
Early menarche	26	14 (60.9)	12 (44.4)	0.382	0.891
Normal menarche	24	9 (39.1)	15 (55.6)		
Menopausal status					
No	25	13 (56.5)	12 (44.4)	0.570	0.798
Yes	25	10 (43.5)	15 (55.6)		
CA 125 level					
Normal	5	0 (0.0)	5 (18.5)	0.054[a]	0.189
High	45	23 (100)	22 (81.5)		
Residual tumor					
≤1 cm	37	21 (91.3)	16 (59.3)	0.024	0.168
>1 cm	13	2 (8.7)	11 (40.7)		
Stage					
Early stage	25	12 (52.2)	13 (48.1)	1.000	1.000
Advanced stage	25	11 (47.8)	14 (51.9)		

Statistical analysis was performed using chi-square test and adjustment of P-value using Benjamin-Hochberg procedure. [a]Statistical analysis use Fisher's Extract test (expected count >20%).

studies suggest these factors may influence the risk of developing OC (42). The current findings revealed that younger patients were more frequently diagnosed with LGSOC than with HGSOC, which is consistent with studies that LGSOC tends to occur at a younger age than HGSOC (9,19,41,43).

Infertility has been cited as a risk factor for OC in several studies (1,2,42). Higher parity is associated with fewer ovulatory cycles, which may reduce the opportunity for tumor development due to ovulation-induced injury of the ovarian epithelium (5,44). Additionally, elevated progesterone levels during pregnancy are considered to protect against ovarian carcinogenesis by inhibiting cell proliferation and promoting apoptosis in ovarian epithelial cells (44). A previous study reported that increased parity correlates with a sustained reduction in the risk of EOC (RR=0.81; 95% CI: 0.77-0.86) (5). Specifically, higher parity was linked to a significant decrease in LGSOC incidence (RR=0.84; 95% CI: 0.76-0.93), while no significant association was found with HGSOC (RR=0.97; 95% CI: 0.92-1.02) (heterogeneity: P=0.01) (45). Conversely, another study reported that having more than two pregnancies significantly reduced the risk of HGSOC (RR=0.25; 95% CI: 0.19-0.50) (46).

Hormonal and reproductive factors are among the most significant additional risk factors for EOC (44,47). The total number of menstrual cycles throughout a woman's life is positively correlated with an increased risk of EOC, highlighting the potential role of repeated ovulation in ovarian carcinogenesis (47). As a result, early menarche and late menopause, which prolong the ovulatory lifespan, can elevate the risk of developing the disease (2,42). Although specific literature on the role of menarche in LGSOC is currently lacking, it has been suggested that both early menarche and late menopause may increase cumulative estrogen exposure, potentially contributing to a higher risk of HGSOC (48,49).

CA 125 is widely recognized as the most important tumor biomarker for the screening and detection of EOC (50). Elevated serum CA 125 levels are observed in ~50% of early-stage tumors, primarily Type I cancers such as LGSOC and in ~92% of advanced-stage cases, predominantly HGSOC (50,51). Higher CA 125 levels have been associated with increased AEG-1 expression, likely due to AEG-1's role in promoting tumor cell proliferation and cancer progression (28,30,34). However, the present findings did not fully align with previous studies, as elevated CA 125 levels were more frequently observed across both groups in our dataset. As a result, the expected cell counts in the statistical analysis exceeded 20%, introducing uncertainty in interpreting the association between CA 125 levels and AEG-1 expression.

Table III. Characterization test based on AEG-1 expression.

Patient characteristics	Total (n=50)	Expression level of AEG-1		Raw P-value	Adjusted P-value
		Low, n (%)	High, n (%)		
Age, years					
≤55	34	8 (53.3)	26 (74.3)	0.191[a]	0.668
>55	16	7 (46.7)	9 (25.7)		
Parity					
Nullipara	19	6 (40.0)	13 (37.1)	0.275	0.641
Primipara	10	1 (6.7)	9 (25.7)		
Multipara	21	8 (53.3)	13 (37.1)		
Menarche					
Early menarche	26	11 (73.3)	15 (42.9)	0.095	0.665
Normal menarche	24	4 (26.7)	20 (57.1)		
Menopausal status					
No	25	7 (46.7)	18 (51.4)	1.000	1,167
Yes	25	8 (53.3)	17 (48.6)		
CA 125 level					
Normal	5	0 (0.0)	5 (14.3)	0.305[a]	0,533
High	45	15 (100.0)	30 (85.7)		
Residual tumor					
≤1 cm	37	11 (73.3)	26 (74.3)	1.000[a]	1.000
>1 cm	13	4 (26.7)	9 (25.7)		
Stage					
Early stage	25	9 (60.0)	16 (45.7)	0.537	0.751
Advanced stage	25	6 (40.0)	19 (54.3)		

Statistical analysis was performed using chi-square test and adjustment of P-value using Benjamin-Hochberg procedure. [a]Statistical analysis use Fisher's Extract test (expected count >20%). AEG-1, Astrocyte Elevated Gene-1.

Table IV. Analysis of differences in AEG-1 expression in ovarian cancer.

Ovarian cancer	Total (n=50)	Expression level of AEG-1		Mann-Whitney U	Sig. P-value	Relative risk (95% confidence interval)	Effect size
		Low, n (%)	High, n (%)				
Low grade	23	11 (73.3)	12 (34.3)	160	0.012	3.228 (1.188-8.776)	0.745
High grade	27	4 (26.7)	23 (65.7)				

Statistical analysis using Mann-Whitney U test. Effect size calculation using Cohen's D. AEG-1, Astrocyte Elevated Gene-1.

HGSOC is characterized by marked aggressiveness in its proliferation, invasion and metastatic behavior, often resulting in diagnosis at advanced stages and a higher likelihood of residual tumor masses >1 cm (52,53). This understanding supports the current findings, which demonstrated that a significantly greater number of HGSOC cases presented with residual tumor sizes >1 cm compared with LGSOC (OR=7.219; 95% CI: 1.399-37.252). While this result is consistent with existing literature, the wide CI suggests that the sample size may have been insufficient. Historically, achieving a maximum residual tumor diameter of <2 cm was considered indicative of successful cytoreductive surgery (54). However, more recent evidence identified that reducing the residual tumor burden to <1 cm provides improved survival outcomes, and it is now widely accepted that complete macroscopic resection (that is, no visible residual disease or R0) offers the greatest survival benefit (53).

AEG-1 contributes to cancer development and progression by activating multiple oncogenic signaling pathways (28,30). Specifically, AEG-1 enhances the PI3K/Akt pathway, promoting the phosphorylation of murine double minute 2 (MDM2) by Akt. This phosphorylation facilitates MDM2's nuclear translocation, leading to the degradation of p53 and enabling continued tumor cell proliferation (30,55,56).

Additionally, the PI3K/Akt pathway is involved in angiogenesis, as Akt activation upregulates HIF-1 expression, which in turn increases VEGF transcription (35,57,58). AEG-1 also plays a key role in cancer cell migration, invasion and metastasis through the activation of the NF-κB pathway (30). Within this pathway, AEG-1 interacts with multiple components, serving as a crucial mediator in NF-κB activation and the subsequent induction of inflammation (59,60). Moreover, by inhibiting retinoid X receptor function, AEG-1 has emerged as a significant regulator of lipid metabolism and the tumor microenvironment during cancer development (59).

According to current theoretical frameworks, AEG-1 is associated with the clinicopathological characteristics of various cancers, including OC. Previous studies investigating AEG-1 expression in OC have demonstrated significant associations with several clinical variables, including age over 55 years (P=0.031), advanced FIGO stage (P<0.001), higher histological grade (P<0.001), elevated CA 125 levels (>35 U/ml, P<0.001), residual tumor size >1 cm (P<0.001) and lymph node metastasis (P=0.027) (30).

By contrast, the present study did not identify a statistically significant association between AEG-1 expression and these clinicopathological characteristics. However, this does not diminish the relevance of the findings. Limitations such as a relatively small sample size and uneven group distribution likely impacted the statistical power, underscoring the need for future studies with larger cohorts or alternative study designs.

Compared with LGSOC, AEG-1 appears to play a role consistent with the more aggressive biological behavior of HGSOC, contributing to increased cancer cell proliferation and invasiveness (28,30,36). HGSOC is clinically recognized for its aggressive progression and poor prognosis (10,11,22). The findings of the present study support this distinction, revealing that AEG-1 expression was significantly higher in HGSOC than in LGSOC (RR=3.228; 95% CI: 1.188-8.776) with the effect size, calculated using Cohen's D, is 0.745. These findings suggest that the aggressive clinical course of HGSOC may be partly driven by elevated levels of AEG-1 expression.

In conclusion, the present study demonstrated a significant difference in AEG-1 expression between HGSOC and LGSOC, with higher levels observed more frequently in HGSOC. These findings contribute to an improved understanding of the molecular distinctions between these two subtypes of EOC and may serve as foundational data for future research. Ultimately, such insights can support more tailored therapeutic approaches and improve patient outcomes and quality of life.

Acknowledgements

The authors are grateful to Dr Sri Ratna Dwiningsih, the supervisor of the study program at the Department of Obstetrics and Gynecology at Airlangga University, for her support in conducting this research. Mr Ary Wahyudiono, a laboratory technician at the Department of Pathology at Universitas Airlangga in Surabaya, assisted in the preparation of paraffin blocks for this investigation. Ms Renata Alya Ulhaq, a medical writer, contributed to the manuscript's substance by ensuring its comprehensiveness.

Funding

No funding was received.

Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

BI and BAT were responsible for the design of the present study, the analysis, and the composition of the manuscript. BI and BU conducted the data extraction and performed an analysis of the results. GA performed the histological examination and image analysis. WS, IY, and PM contributed essential revisions to the document. BI, BAT and BU confirm the authenticity of all the raw data. All authors contributed to the interpretation of data and the revision of the manuscript, read and approved the final version of the manuscript.

Ethics approval and consent to participate

The present study was approved by the Institutional Review Board (IRB) of Dr Soetomo Hospital Surabaya (approval no. 1641/LOE/301.4/2/IV/2024; Surabaya, Indonesia). Data management adhered carefully to patient confidentiality and privacy regulations. Anonymized and de-identified data were used to uphold participant rights and privacy. The IRB approved the use of anonymised patient data after careful evaluation of the limited associated risks. Acquiring written informed consent was waived by the IRB of Dr. Soetomo Hospital Surabaya.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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