

Research Article

Prevalence of Appendical Metastasis in Primary Surgery of Ovarian Epithelial Cancer

Prevalensi Metastasis Apendiks Pada Bedah Primer Kanker Epitel Ovarium

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Abstract

Objective: To determine the prevalence of metastasis to appendix from primary surgery of ovarian epithelial cancer at National General Hospital Dr. Cipto Mangunkusumo (RSCM), Indonesia.

Methods: A cross sectional study was done using ovarian epithelial cancer patient medical record whose primary ovarian cancer and appendectomy surgery were conducted on July to December 2019 at RSCM. Patients without appendix histopatology result and previous chemotherapy were excluded in this study. Consecutive method and random sampling were used in this study.

Results: A total of 80 subjects were included in this study. Subjects have average age of 48 years old. Out of all samples, 43 samples (53.8%) were defined as stage I patient, 7 subjects (8.8%) as stage II, 30 subjects (37.5%) as stage III, and none as stage IV. Appendectomy were done and eight subjects (10%) experienced metastasis to appendix. A total of 19 subjects (23.8%) had chronic appendicitis and 53 subjects (66.3%) did not have metastasis to the appendix. Among eight subjects having appendix involvement, 4 had mucinous histology, 2 serous, and 2 endometrioid. Six out of eight were diagnosed at clinical stage III and two were diagnosed at stage I.

Conclusions: The prevalence of appendix metastases from primary surgery in ovarian epithelial cancer at RSCM was 10%. Based on this research, appendectomy can be considered on ovarian cancer surgery.

Keywords: appendix, metastasis, ovarian cancer.

Abstrak

Tujuan: Mengetahui prevalensi metastasis kanker epitelial ovarium ke apendiks pada pembedahan primer kanker epitelial ovarium di Rumah Sakit Umum Pusat Nasional Dr. Cipto Mangunkusumo (RSCM), Indonesia.

Metode: Penelitian ini merupakan studi potong lintang menggunakan data rekam medis pasien kanker ovarium epitelial yang menjalani pembedahan primer dan apendektomi pada bulan Juli hingga Desember 2019 di RSCM. Pasien tanpa histopatologi apendiks atau pernah dilakukan kemoterapi sebelumnya dieksklusi dari penelitian. Digunakan metode pengambilan sampel secara acak.

Hasil: Didapatkan 80 subjek penelitian yang diikutsertakan dalam penelitian. Dari 80 subjek penelitian, didapatkan rerata usia 48 tahun. Sebanyak 43 subjek (53,8%) didiagnosis dengan stadium I, 7 subjek (8,8%) sebagai stadium II, 30 subjek (37,5%) stadium III. Dari 80 subjek yang menjalani apendektomi, didapatkan 8 subjek (10%) anak sebar ke apendiks, 19 subjek (23,8 %) apendisitis kronis, 53 subjek (66,3%) tidak terdapat anak sebar. Dari 8 subjek yang terdapat anak sebar ke apendiks dengan temuan histologi 4 musinosum, 2 serosum, 2 endometrioid. Sebanyak enam dari delapan subjek terdiagnosis pada stadium klinis stadium III dan dua lainnya pada stadium klinis satu.

Kesimpulan: Prevalensi metastasis apendiks pada operasi primer kanker ovarium epitelial di RSCM adalah sebesar 10%. Berdasarkan hasil penelitian ini, apendektomi dapat dipertimbangkan dilakukan pada pembedahan baik stadium awal maupun stadium lanjut.

Kata kunci: apendiks, kanker ovarium, metastatis.

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INTRODUCTION

Ovarian cancer is one of the leading causes of morbidity and mortality of women in the world. It is the 7th most prevalent cancer in women and the 9th most prevalent of all cancer.¹ Incidence of ovarian cancer is predicted to be 3.4% per year with 4.3% mortality rate.¹ Over 90% of all malignant ovarian cancer is epithelial ovarian cancer. Epithelial ovarian cancer consists of various subtypes, such as serous, endometrioid, clear cell, mucinous, transitional cell, undifferentiated, and not classified. Federation of Gynecology and Obstetrics (FIGO) in its guideline recommends surgical staging on ovarian cancer through finding during exploration.² Optimally performed surgical staging is the key to treatment after surgery which supports accurate prognosis, better chemotherapy outcome, and higher survival rate by removing all tumour and its metastasis.

Appendix is an intraperitoneal organ prone to be a site of metastasis of epithelial ovarian cancer due to its anatomical site near paraclioica space where ascites could build-up, especially in right ovarian cancer.³ Appendectomy is routinely done in patients with epithelial ovarian cancer subtype mucinous in order to exclude appendix carcinoma. There were some controversies regarding the decision of routine appendectomy in other subtypes of cancer, although previous study has shown that appendix pathologic examination would promote better staging and optimal cytoreduction.⁴ There was no previous research on metastasis to the appendix on epithelial ovarian cancer in our institution. Therefore, this study aims to determine the prevalence and characteristic of appendical metastasis of ovarian cancer undergoing primary surgery.

METHODS

A descriptive research with cross-sectional method with was done in National General Hospital Dr. Cipto Mangunkusumo Jakarta on July to December 2019. The study population were all ovarian cancer patients undergoing primary surgery with concurrent appendectomy. Patients without appendix histopathology and previous chemotherapy were excluded from this study. Total sampling method was done in regards to small prevalence in the population. Patients were then divided into metastasis and

non-metastasis group. Baseline characteristics were analyzed and compared. Ethical clearance was issued from the ethical committee of Faculty of Medicine, Universitas Indonesia with letter number KET-636/UN2.F1/ETIK/PPM.00.02/2019.

RESULTS

During the course of the study, there were 80 ovarian cancer patients undergoing primary surgery with appendectomy with the average age of 48.6 years. The proportion of metastasis to the appendix was 10% (8 subjects). Among 53 (66.3%) patients who did not have metastasis to the appendix, 19 (23.8%) patients were found to have chronic appendicitis. Baseline characteristics of subjects can be found in Table 1.

Table 1. Baseline Characteristics of Subjects

Variables	N = 80
Age	48.6 (25 – 72)
Clinical Stage	
I	43 (53.8)
II	7 (8.8)
III	30 (37.5)
IV	0 (0.0)
Subtype	
Brenner	1 (1.3)
Mucinous	22 (27.5)
Serous	12 (15)
Endometrioid	17 (21.3)
Clear Cell	26 (32.5)
Mixed	2 (2.5)
Metastasis to the Appendix	
Positive	8 (10.0)
Negative	72 (90.0)

Subjects of this study were then categorized into two groups, namely positive metastasis to the appendix group {metastatis (+) group} and negative metastasis to the appendix group {metastatis (-) group}. Characteristics of subjects in each group can be found in Table 2.

Table 2. Characteristics of Subjects

Variables	Study Groups	
	Metastasis (+)	Metastasis (-)
Age (years)		
< 50	3 (3.75)	40 (50)
> 50	5 (6.25)	32 (40)
Clinical Stage		
I	2 (2.5)	41 (51.3)
II	0	7 (8.8)
III	6 (7.5)	24 (30)
IV	0	0

Among 8 patients having metastasis to the appendix, some subjects were having more than one subtype of cell. Subtypes of cancer cell having metastasis to the appendix can be found in table 3.

Table 3. Subtype Distribution of Metastasis Ovarium Cancer to Appendix Metastasis

Subtype of Histopathology	Stage I	Stage II	Stage III
Mucinous	2	0	2
Serous	0	0	2
Endometrioid	0	0	2

DISCUSSION

In this study, it was found that the average age of subjects in this study was 48.6 years, lower than the average age of various studies showing that ovarian cancer patients having primary surgery would have an average age of 50 to 70 years old due to the lack of symptoms and compliance of older patients, probably delaying the treatment necessary.^{5,6} It was also found that the most prevalent subtypes in ovarian cancer in this study was clear cell subtype with proportion of 32.5%, followed by mucinous (27.5%), endometrioid (21,3%), serous (15%), and mixed type (1.3%). Cell subtypes is one of prognostic factors in epithelial ovarian cancer, with clear cell subtypes having worse prognosis due to lower chemotherapy response.⁷ In earlier stage, clear cell subtype would have similar prognosis and even higher survival rate than serous type. However, it was not until advanced stage that clear cell subtype would give worse outcome to the patient.⁷

Epithelial ovarian cancer is mainly divided into five subtypes according to its prevalence, namely high-grade serous carcinoma (HGSC), endometrioid carcinoma (EC), clear cell carcinoma (CCC), mucinous carcinoma (MC), and low-grade serous carcinoma (LGSC). Usually, HGSC would be diagnosed much later than other subtypes, in accordance to the finding this study and previous studies.^{8,9} In this study, 50% of serous subtype were founded in advanced tumour stage, much higher than mucinous (31%), clear cell (37,5%), endometrioid (3.5%), and Brenner (0%).

Ovarian cancer spreads primarily in the abdominal and pelvic cavity. Although patients with early clinical stages usually do not have involvement with the appendix, evaluation of the appendix is needed during surgery because the involvement of the appendix will make cancer grading increase and require adjuvant treatment.^{4,9,10} Appendectomy should also be done in ovarian cancer patients due to its anatomical site, where ascites could build-up especially in right ovarian cancer and further increase the rate of metastasis.¹⁰

It was discovered that 10 per cent of the subjects of this study experienced involvement from the appendix. This percentage is still lower than other studies which stated that appendix involvement was 15% or even 29%.^{4,1} Ovarian epithelial cancer has a very poor prognosis at an advanced stage regardless of the subtype of cancer. In our study, the spread to the appendix was more severe at stage 3-4 (advanced stage) with a proportion of 20% compared to stage 1-2 (early stage) with a percentage of 4 %. Higher percentage of metastasis in this study is related to higher stadium at the time of diagnosis.

Limitation of this study is the method used which is retrospective cohort to determine the prevalence of appendical metastasis in ovarian cancer. Further studies should be done prospectively to have higher degree of causality.

CONCLUSIONS

The prevalence of metastasis to the appendix in ovarian cancer patients having primary surgery and concurrent appendectomy in this study is 10%. Ovarian cancers with appendix metastasis were made of various subtypes and clinical stages.

DECLARATIONS

This study was acknowledged by Ethical Committee for Medical Research of Faculty of Medicine, University of Indonesia. The authors declare that they have no competing interests.

REFERENCES

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*. 2015;136(5):E359-86.
2. Bhatla N, Denny L. FIGO Cancer Report 2018. *Gynecol Obstetr*. 2018;143(2):2-3.
3. Beşe T, Kösebay D, Kaleli S, Öz AU, Demirkiran F, Gezer A. Appendectomy in the surgical staging of ovarian carcinoma. *Int J Gynecol Obstet*. 1996;53(3):249-52.
4. Sarı Mustafa Erkan, et al. "Risk factors for appendiceal involvement in women with epithelial ovarian cancer. *J Turk Ger Gynecolo Associat*. 2017; 18(3): 116.
5. Coburn SB, Bray F, Sherman ME, Trabert B. International patterns and trends in ovarian cancer incidence, overall and by histologic subtype. *Int J Cancer*. 2017;140(11):2451-60.
6. Wallace SK, Lin JF, Cliby WA, Leiserowitz GS, Tergas AI, Bristow RE. Refusal of Recommended Chemotherapy for Ovarian Cancer: Risk Factors and Outcomes; a National Cancer Data Base Study. *Journal of the National Comprehensive Cancer Network : JNCCN*. 2016;14(5):539-50.
7. Mackenzie R, Talhouk A, Eshragh S, Lau S, Cheung D, Chow C, et al. Morphologic and Molecular Characteristics of Mixed Epithelial Ovarian Cancers. *Am J Surg Pathol*. 2015;39(11):1548-57.
8. Auersperg N. The origin of ovarian carcinomas: a unifying hypothesis. *International journal of gynecological pathology : Official J Int Soc Gynecol Pathol*. 2011;30(1):12-21.
9. Bamias A, Sotiropoulou M, Zagouri F, Trachana P, Sakellariou K, Kostouros E, et al. Prognostic evaluation of tumour type and other histopathological characteristics in advanced epithelial ovarian cancer, treated with surgery and paclitaxel/carboplatin chemotherapy: cell type is the most useful prognostic factor. *Eur J Cancer (Oxford, England : 1990)*. 2012;48(10):1476-83.
10. Ozcan A, Töz E, Turan V, Sahin C, Kopuz A, Ata C, et al. Should we remove the normal-looking appendix during operations for borderline mucinous ovarian neoplasms?: A retrospective study of 129 cases. *Int J Sur*. 2015;18:99-103.