Case Report

Resolution of Ethical Conflicts between Medical Indications and Patient Preferences in Case of Unmarried Woman with Ovarian Cancer

Penyelesaian Konflik Etika antara Indikasi Medik dan Preferensi Pasien pada Kasus Perempuan yang belum Menikah dengan Kanker Ovarium

Taufik Suryadi^{1,2}, Putri Irmayani³, Kulsum Kulsum⁴

¹Department of Forensic Medicine and Medicolegal ²Ethics and Medicolegal Consultant ³Department of Obstetric and Gynecology ⁴Department of Anesthesiology and Intensive Care Faculty of Medicine Universitas Syiah Kuala Banda Aceh

Abstract

Objectives: To resolve ethical conflicts in medical decision making in unmarried patients with a diagnosis of ovarian cancer. The ethical issue in this case is the main operative management in cases of ovarian cancer, namely removal of the uterus and both ovaries even though the patient is not married and has never been pregnant. The opportunity for patients to get pregnant no longer exists, so there is an ethical conflict between medical indications and patient preferences.

Methods: This case report is about an unmarried woman 38year with a diagnosis of ovarian cancer. This patient initially underwent right salfingooophorectomy surgery. Anatomical pathology results found adenocarcinoma serosum ovarii. The patient underwent chemotherapy for 3 cycles. Then the patient was re-operated with a planned debulking interval laparotomy.

Discussion: From the aspect of patient indications, the results of combination treatment between surgery and chemotherapy have shown a marked increase in the survival rate of patients in five years. The choice of performing a debulking interval laparotomy is a difficult choice. The patient's preference to get pregnant will be difficult to accept, but it can be accommodated by improving the quality of life and paying attention to humanism, social and cultural aspects of its contextual features.

Conclusion: Clinical ethical considerations related to uterine removal in unmarried patients is a matter of debate. Clinical ethical theory namely quality of life, patient preferences, medical indications, and contextual features are beneficial in medical decision making.

Keywords: debulking intervals, ethical conflicts, medical indications, ovarian cancer, patient preferences.

Abstrak

Tujuan: Untuk menyelesaikan konflik etik dalam pengambilan keputusan medik pada pasien yang belum menikah dengan diagnosis kanker ovarium. Isu etik pada kasus ini yaitu manajemen operatif utama pada kasus kanker ovarium yaitu pengangkatan uterus dan kedua ovarium padahal pasien belum menikah dan belum pernah hamil. Kesempatan untuk pasien untuk hamil tidak ada lagi sehingga terjadi pertentangan etik antara indikasi medik dengan preferensi pasien.

Metode: Laporan kasus ini tentang seorang pasien perempuan yang belum menikah, berusia 38 tahun dengan diagnose kanker ovarium. Pasien ini awalnya dilakukan operasi salfingoooforektomi kanan. Hasil patologi anatomi ditemukan adenokarsinoma serosum ovari. Pasien menjalani kemoterapi sebanyak 3 siklus. Kemudian pasien dilakukan operasi kembali yang direncanakan tindakan laparotomi interval debulking.

Diskusi: Dari aspek indikasi pasien, hasil pengobatan kombinasi antara pembedahan dan kemoterapi telah menunjukkan peningkatan survival rate yang nyata pada pasien dalam lima tahun. Pilihan melakukan tindakan laparotomi interval debulking merupakan pilihan sulit. Preferensi pasien untuk dapat hamil akan sulit dikabulkan, namun dapat diakomodir dengan peningkatan kualitas hidup dan memperhatikan aspek humanism, sosial dan kultural pada fitur kontekstualnya.

Kesimpulan: Pertimbangan etik klinik yang berhubungan dengan pengangkatan rahim pada pasien yang belum menikah merupakan masalah yang diperdebatkan. Teori etika klinis yaitu indikasi medis, preferensi, kualitas hidup dan fitur kontektual sangat membantu dalam pengambilan keputusan medis yang etis.

Kata kunci: indikasi medis, interval debulking, kanker ovarium, konflik etik, preferensi pasien.

Correspondence author. Taufik Suryadi. Department of Forensic Medicine and Medicolegal Faculty of Medicine Universitas Syah Kuala. Banda Aceh. Email; taufiksuryadi@unsyiah.ac.id Received: October, 2021, Accepted: August, 2023 Published: October, 2023

INTRODUCTION

The medical profession involves clinical skills and decision-making in services aimed at protecting and restoring human well-being. A doctor must make clinical judgments gained through practice, experience, knowledge, and ongoing critical analysis. Two-way communication is very important in the doctor-patient relationship.¹

Important doctor-patient aspects of communication include developing doctorpatient interpersonal relationships, doctors listening to all patient problems holistically, doctors providing as much information as possible to patients, and making treatment management plans for patients. Good and effective doctorcommunication increases patient patient confidence in doctors. It will indirectly affect the level of patient satisfaction and treatment outcomes, such as symptom improvement and adherence to medical treatment. Therefore, from a clinical standpoint, good and directed communication is the main capital of the doctorpatient relationship and can increase trust and service to patients effectively.^{1,2}

In making clinical decisions, doctors are often faced with dilemma cases between the patient's medical problems and ethical decisions regarding the patient's condition. Therefore we need four main ethical principles, namely beneficence, nonmaleficence, autonomy, and justice in making medical decisions. In patient care situations, there is often a conflict between the ethical principles themselves, especially between the principles of beneficence and autonomy. Each of the four ethical principles must be considered a prima facie obligation that must be fulfilled.³

One of the dilemmas faced by doctors is decision making in cases of ovarian cancer in unmarried women. Ovarian cancer can occur at any age. Ovarian cancer is one of the leading causes of death in the United States. In 2015 there were an estimated 21,290 cases of ovarian cancer and 14,180 of them ended in death. The average survival rate of ovarian cancer patients is only around 30%, despite chemotherapy and surgery. This is because ovarian cancer itself is a "silent killer", resulting in a delay in diagnosis. Ovarian cancer has non-specific symptoms such as discomfort in the stomach, nausea, vomiting, urinary disorders, so it is often mistaken and is considered a dyspepsia problem.⁴

The National Cancer Institute reports that

young patients have a mortality rate of 1.0 per 100,000. For patients over 50 years old, the mortality rate is 25.5 per 100,000.⁵ Ovarian cancer can occur at any age. Ovarian cancer occurs 6%-11% in premenopausal age and 29%-35% in malignant postmenopausal age. Ovarian cancer remains the third most common gynecologic malignancy with the highest mortality rate in developed countries. Only 20% of ovarian cancers are diagnosed at an early stage if the disease is confined to the ovaries.^{6,7}

In general, patients come with advanced stage conditions so that the mortality rate is higher (75%), where there has been metastasis to other organs such as the peritoneal cavity and even to more distant organs. Ovarian cancer metastases can be through direct spread from the ovaries or through the fallopian tubes to surrounding organs such as the large intestine or bladder, metastases can also occur when cancer cells are separated from the primary tumor. Tumor cells exfoliate in the peritoneal cavity and adhere to the peritoneal fluid, causing expansion in the abdominal cavity. Metastasis of this type is often suspected as ascites, especially in advanced ovarian cancer.^{6,7}

In this case, the doctor is faced with a dilemma between carrying out actions according to medical indications based on the patient's diagnosis, namely ovarian cancer and the patient's preference for not having surgery because she is not yet married. The patient's hope to get pregnant in the future is very high, but it seems difficult to be granted so that the doctor must provide the best solution to overcome this dilemma. Consideration of clinical ethics by balancing quality of life, medical indications, contextual features and patient preferences can help resolve this dilemma.

In this case, a dilemmatic conflict will be discussed, namely an unmarried woman and diagnosed with ovarian cancer. The ethical issue in this case is the main operative management in cases of ovarian cancer, namely removal of the uterus and both ovaries with the patient's desire to remain pregnant.

CASE

This case report is about a female patient, unmarried. 38 years old who initially came with complaints of an enlarged stomach that had been experienced since 3 months before being admitted to the hospital. The patient claimed to

have regular menstrual cycles and denied pain during menstruation. There were no complaints of bleeding from the birth canal, there were no complaints of prolonged menstruation, complaint of smelly vaginal discharge were denied. From the physical examination, the general condition was good, compos mentis consciousness, blood pressure 120/70 mmHg, pulse 76 times per minute, body temperature 36.5 0C, breathing 18 times per minute, from general status examination, there was no anemia in the eyes or conjunctiva or sclera icteric, the abdomen does not appear enlarged, there is scar tissue from surgery, with no shifting dullness, no undulation, no tenderness. From the gynecological status, inspection found the vulva urethra is calm. Vaginal toucher examination cannot be done because the patient is not married. Rectal toucher examination found smooth rectal mucosa, tight anal sphincter tone, no bleeding, no palpable intraluminal mass. From the laboratory examination, it was found that hemoglobin 10,3 g/dl, hematokrit 32 %, leukosit 12000/mm3, trombosit 284000/mm3, blood sugar 92 mg/dL, Natrium 146 mEg/L, Kalium 3,9 mEq/L, Cl 106 mEq/L. Ca125: 44.9, SGOT/SGPT: 133/370, Albumin: 4.8. From these laboratory results, it can be concluded that there is an increase in the tumor marker ca 125 in patients.

An ultrasound examination was performed. From the results of ultrasound, it was found that the uterus was anteflexed with a size of 7x7x5 cm. The positive endometrial line is 11.7 mm thick. The left ovary is within normal limits, there is no mass picture. The right ovary is difficult to assess the post-laparotomy effect of right salpingoophorectomy. The patient has had a dextra salfingooophorectomy surgery on January 1, 2021 previously with the result of anatomical pathology, namely adenocarcinoma serosum ovarii. Then the patient underwent chemotherapy for 3 cycles. Then the patient underwent surgery again. The patient was planned for a debulking interval laparotomy. There was an ethical conflict in the case of an unmarried female patient who was diagnosed with ovarian cancer. The ethical issue in this case is the main operative management in cases of ovarian cancer, namely removal of the uterus and both ovaries even though the patient is not married and has never been pregnant. The opportunity for patients to become pregnant no longer exists, resulting in an ethical conflict between medical indications and patient preferences.

DISCUSSION

In this case there is an ethical conflict, namely the patient is an unmarried woman and was diagnosed with ovarian cancer. The patient had had surgery to remove one ovary and the results of anatomical pathology examination were malignant. Then the patient underwent 3 cycles of chemotherapy and a second surgery was planned, namely interval debulking of the tumor, where the procedure included removal of the contralateral uterus and ovaries and resection of all visible tumor masses. In an effort to overcome this problem, an ethical dilemma solution is used based on the clinical ethics theory proposed by Jonsen and Siegler with systematic consideration of medical indications (including advantages and disadvantages of treatment), patient preferences (including autonomy or protection and patient capacity to choose), patient's quality of life (patient sees the expected outcome, prospective interventions from his life situation, and the impact of his future quality of life), contextual features (equity issues).8 Clinical ethical decision making can be seen in Figure 1.

Medical Indication

Medical indications in patients can be done using the principles of beneficence and nonmaleficence. The principle of beneficence means that therapy must provide the maximum benefit to the patient both medically and ethically, while non-maleficence means that it does not cause harm to the patient. Determination of medical indications is done by looking at the diagnosis and medical problems of the patient's disease, including answering questions such as: What about the patient's medical history? What is the diagnosis and prognosis of the patient's disease? What are the benefits of the treatment? What is the probability of success and failure of the therapy process? Are there other plans if this therapy doesn't work?⁸

The main management for early-stage epithelial ovarian cancer is surgical staging. Surgical staging measures in early-stage ovarian cancer include peritoneal washings, total abdominal hysterectomy, and salpingooophorectomy, inspection of all abdominal organs and peritoneal surfaces, biopsy of suspicious areas, namely the posterior cul-desac, paravesica, both pelvic walls and paracolic, omentectomy, bilateral paraaortic and pelvic lymphadenectomy and appendectomy in cases of mucinous lesions. Meanwhile, for advanced ovarian cancer, cytoreductive surgery or tumor debulking is performed, namely resection of the entire tumor mass, both primary and metastatic. Cytoreduction surgery for ovarian cancer usually includes total abdominal hysterectomy (TAH) or supracervical hysterectomy (SCH), bilateral salpingo-oophorectomy (SOB), omentectomy, and resection of any metastatic lesion.^{9,10}

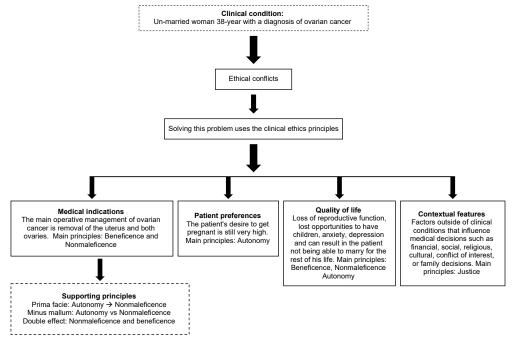


Figure 1. Schematic for solving ethical conflicts

It has been shown that patients with ovarian cancer can have atypical symptoms. The general public's knowledge of ovarian cancer is still low. In addition, the symptoms of ovarian cancer are often mistaken for symptoms of gastrointestinal disease. The survival of women with ovarian cancer is largely determined by stage women with stage I or II cancer have a five-year survival rate of 50%-90%. Meanwhile, the survival of women with advanced disease decreased to about 30%. 7,10,11.

The classification of ovarian cancer according to the International Federation of Gynecology and Obstetrics (FIGO) is described in table 1: ^{9,10}

Stadium	Disease conditions	
1A	Stage I is limited to the ovaries or fallopian tubes The tumor is only in one ovary or fallopian tube, the tumor capsule is intact or not ruptured, there is no tumor growth on its surface, ascitic fluid or fluid flushing in the lining of the abdomen (peritoneum) no tumor cells	
1B	Tumor confined to two ovaries or fallopian tubes, no tumor growth on their surface, no tumor cells in ascites or washings of the ovarian cavity	
1C	Tumor confined to one or two ovaries with one of the following factors: IC1 tumor capsule ruptured due to surgery,	
	IC2 tumor capsule ruptured before surgery or tumor growth on the surface of the ovary or fallopian tube, IC3 there are tumor cells in the ascitic fluid or in the peritoneal fluid rinses	
IIA	Stage II tumor in one or both ovaries or fallopian tubes with extension in the pelvic cavity The tumor extends to the uterus and/or into the tubes	
IIA IIB	Tumor extends to other intraperitoneal pelvic organs	
	Stage III tumor is present in one or both ovaries or fallopian tubes with extension of the tumor in the peritoneal cavity beyond the pelvis and/or regional lymph node metastases	
IIIA	Stage IIIA1, retroperitoneal spread, IIIA1(i) metastases 10 mm, IIIA (ii) metastases > 10 mm, IIIA2 microscopic spread outside the pelvis	
IIIB	Macroscopic spread outside the pelvis, the size of the injury spread 2 cm	
IIIC	Macroscopic spread outside the pelvis, injury spread >2 cm and spread to lymph nodes. Stage IV spread beyond the peritoneal cavity	
IV A	Pleural effusion with positive cytology, stage IVB: parenchymal metastases and metastases to extrabdominal organs.	

Ovarian cancer patients have the lowest survival rate of all other cancers, which is 30-50% in the last five years. In comparison, breast cancer patients have a survival rate of more than 80 percent. In a retrospective survey it was found that 77% of ovarian cancer patients experienced abdominal symptoms, namely bloating, pain; 70% gastrointestinal symptoms, namely indigestion, constipation, and nausea; 58% of symptoms involving pain were abdominal pain, coitus pain, and back pain; 50% psychological symptoms namely fatigue, anorexia, and weight loss; 34% of urinary disorders, namely increased frequency of urination and difficulty holding urination (incontinence); and 26% of symptoms related to abnormal bleeding outside the menstrual cycle and a palpable mass in the abdomen.^{7,12}

Debulking interval laparotomy or cytoreductive interval is the surgical option in advanced cancer. In principle, this operation is performed after chemotherapy. This procedure can be applied to the following situations; patients who underwent an initial exploratory laparotomy but were unable to remove the entire mass of the primary tumor due to adhesions, and patients who were deemed unsuitable for primary cytoreductive surgery due to unfavorable general conditions, such as disease comorbid or extensive disease metastases.10

The results of combination treatment between surgery and chemotherapy have shown a marked increase in the survival rate in patients over a period of five years, but death can still occur due to factors of metastatic lesions, non-adherence in chemotherapy discipline, and chemotherapy drug resistance. The use of chemotherapy is also limited because the dose-related toxicity of chemotherapy drugs can interfere with the patient's quality of life.^{7,13}

Ethical aspects in clinical situations often lead to ethical dilemmas in the form of dilemmas between medical indications versus patient preferences, medical indications versus quality of life and medical indications versus contextual descriptions.8 In this case, there is an ethical conflict between medical indications vs patient preferences, namely:

 Table 2. Ethical Conflicts between Medical Indications versus Patient Preferences

Medical indications	Patient preferences
Patients diagnosed with ovarian cancer. The treatment to be taken on the patient is the tumor debulking interval. The goal of treatment for patients is to reduce complaints caused by primary tumors or metastases. This treatment is expected to increase the survival rate of this patient. Patients are still required for regular clinical evaluation, laboratory and ultrasound examinations.	 The patient is not married and wants to get pregnant someday. The patient is 38 years old and able to decide his own life matters. The patient has the right to make the best choice for her own body. The patient has been given an explanation of his illness, treatment options and side effects regarding the action taken. The patient has understood and is willing to sign the informed consent form. Patients can cooperate well for postoperative evaluation and follow-up chemotherapy.

Patient Preference

Preference is based on several options, namely whether the patient is mentally prepared and competent enough to receive a legal operation? Has the patient been informed about the benefits and dangers, does he or she understood it, and has he or she given informed consent? Are there any conditions that make the patient more likely to be disabled? Does the patient indicate something he or she prefers? Is the patient reluctant or unable to participate with the prescribed therapy? If so, ask the patient to explain why. Furthermore, does the patient's right to choose depend on the patient's religion and ethnicity?⁸

This approach to ovarian cancer can restore life expectancy in patients with this disease.¹² The Hopkins study found that in premenopausal women with a diagnosis of ovarian cancer, removal of both ovaries (oophorectomy) induces a sudden decrease in estrogen and androgens and general symptoms, and others such as hot flushes. Menopause can then cause vaginal wall atrophy, vaginal dryness, and increased local sensitivity to pain. These factors contribute to dyspareunia or pain during coitus. The fear that accompanies pain can also reduce sexual response. Decreased androgens can be associated with reduced sexual arousal. Chemotherapy can also cause side effects including fatigue, alopecia, and neuropathy, all of which can also negatively impact body image

and sexuality. Hopkins also stated that there are five factors that quite influence sexual function in ovarian cancer survivors, namely: disinterest in sex, physical disorders, not having a partner, fatigue, and partners who are not interested in having sex. The patient's desire to get pregnant is still very high. However, it is difficult for doctors to accept this considering the severity of the patient's clinical condition. National Ovarian Cancer Coalition , issues related to the quality of life of ovarian cancer patients include: ^{14,15}

Treatment-related side effects consisting of: Surgery-related side effects i.e. loss of fertility, menopause due to surgery, sexual worries, intestinal obstruction, and ostomy care. Side effects related to chemotherapy are side effects on the digestive system such as nausea, vomiting, loss of appetite, constipation, and diarrhea; peripheral neuropathy in the form of tingling and numbress; side effects on the brain i.e. being forgetful; hair loss; disorders of blood cell formation in the form of anemia and thrombocytopenia; and easily feel tired. Depression, anxiety, and distress. In some women with ovarian cancer, strategies for managing depression, anxiety, and distress are exercise, relaxation, going out and doing fun things.Financial problem can be a source of stress for women with ovarian cancer.^{14,15}

The basic moral principles serve as an analytical framework which can then serve as guidelines for professional ethics, namely; 3,16-19 Respect for patient decisions (Autonomy). Adult patients have the choice to accept or refuse surgery. Even if the choice is not the best, the decision must be respected. The patient has the right to choose what can be done to his/her body. Norms of avoiding harm/harmness (Non-Maleficence). A doctor must also be aware of the dual effects of therapy, where a very good treatment can inadvertently cause harm to the patient's body. This means that any medical procedure can have consequences. The basic principle of medical ethics is to avoid things that can cause harm to patients and every health worker must be fully aware of this norm. The norm of giving the most benefits and causing the least harm (Beneficence). Each scenario should be evaluated based on the individuality of the patient. This condition implies that what is beneficial to one patient may not be beneficial to another. All health workers must understand that improving the patient's health is by doing the best in the situation according to the wishes of each patient. The norm of justice for the right of every individual to their fair and equitable health care and the risks involved (Justice). Moral principles that emphasize fairness and justice in behavior, do not discriminate against a patient based on ethnicity, race, culture, religion, level of wealth and occupation.

Quality of Life

Quality of life describes the patient's quality of life after treatment. How is the patient's condition now or in the future?, is the patient's next life still the same when compared to before treatment? What is the patient's chance of returning to quality of life, with or without therapy? Can the patient experience medical, emotional, or social problems as a result of the treatment? Are there biases that could cast doubt on the health care provider's assessment of a patient's quality of life? Is there a logical reason to continue treatment? Are there strategies for comfort and palliative care?⁸

Removal of the uterus in an unmarried patient has a major life impact. A woman will lose reproductive function, the opportunity to have children, anxiety, depressed and can result in the patient not being able to marry for the rest of her life. In this case, psychological and mental support is needed for the patient from friends, family and people closest to the patient. The theoretical model in ovarian cancer patients describes four domains of quality of life (QOL) including physical and symptom well-being, social, mental, and spiritual well-being. Physical nicely-being and signs and symptoms include bodily electricity/fatigue, sleep and relaxation, basic physical fitness, menstrual changes, pain/neuropathy, urge for food, and nausea/ constipation. Social nicely-being includes a circle of relatives (family) pressures, roles and relationships, sexuality/fertility, isolation, budget, painting, social aid, and fear of future generative diagnosis. Mental nicely-being consists of management, anxiety, despair, happiness, worry of recurrence or metastasis, cognition/attention, difficulties with analysis or treatment, coping, appearance/self-concept, and value. In the end, the area of spiritual properly-being consists of wisdom from illness, religiosity, spiritual lifestyles, hope, uncertainty, and existence's motive/task.²⁰

Several studies have stated that there is a relationship between decreased quality of life and ovarian cancer. The subgroup of women with ovarian cancer diagnosed as having a better threat of experiencing distress related to the mental measurement. The researchers adviced for routine mental screening and monitoring, identify, and intervene in women who are at high risk for psychological distress due to cancer. Other studies have shown that women with ovarian cancer are at risk for mental problems due to their diagnosis. It is recommended to conduct early screening to overcome mental problems.²⁰

In this condition, ethical considerations can be made with a prima facie approach by prioritizing the interests of the patient, namely surgical removal of the uterus and both ovaries so that the cancer does not spread to other body parts that can endanger the patient. In this case the doctor won the principle of nonmaleficence (preventing harm to the patient) over the patient's autonomy, even though in the end the patient had no chance of getting pregnant, or it could be the minus mallum approach by choosing the least bad thing, i.e. there is still life expectancy if an operation is performed with a better survival rate, it has a minimal risk compared to the patient dying without any medical procedure. Removal of the uterus in an unmarried patient is a bad way because it will injure the patient, the procedure certainly makes wounds on the patient's body, but the goal is good, namely the health and safety of the patient, this condition is called the double effect principle. The patient's family already understands this information and gives consent and accepts whatever will happen to the patient. 8,21

Contextual Features

Medical decisions are not only decided by doctors and patients but also must consider other aspects such as socio-cultural, belief, religion, and finance. The related contextual features are: Are there any family problems that might influence the decision to choose treatment? Are there problems with the data sources (doctors and nurses) that might influence treatment selection decisions? Are there financial or other economic issues? Are there religious and cultural considerations? Are there limits to the patient's trust in the therapeutic management team? Is there a problem with resource allocation? How does the law affect treatment decisions? Is there clinical research or ongoing learning? Is there a conflict of interest in the health department in the decision making of an institution?⁸ In this patient there was no conflict of interest in decision making. There are no family problems that affect treatment decision making, there are no financial problems because the patient is covered by the Indonesia of Health Social Security Administration Agency (Badan Penyelenggara Jaminan Sosial (BPJS) Kesehatan) and there are no barriers to religious and cultural factors.

CONCLUSIONS

The patient underwent debulking interval laparotomy even though the patient was not married. This procedure is the main management of ovarian cancer. Clinical ethical considerations related to uterine removal in unmarried patients is a matter of debate. The principles of clinical ethics, namely contextual features, medical indications, quality of life and patient preferences are very helpful in making ethical clinical decisions. The patient has been given the best possible explanation of the procedure performed and agreed to it.

REFERENCES

- 1. Kienle GS, Kiene H. Clinical judgement and the medical profession. J Eval Clin Pract. 2011;17(4): 621–7.
- Chandra S, Mohammadnezhad M. Doctor-patient communication in primary health care: A mixed-method study in Fiji. Int J Environ Res Public Health. 2021;18(14): 1-12.
- 3. Varkey B. Principles of clinical ethics and their application to practice. Med Princ Pract. 2021;30(1):17–28.
- Yeung TL, Leung CS, Yip KP, Yeung CLA, Wong STC, Mok SC. Cellular and molecular processes in ovarian cancer metastasis. A review in the theme: Cell and molecular processes in cancer metastasis. Am J Physiol - Cell Physiol. 2015;309(7):C444–56.
- 5. Lengyel E. Ovarian cancer development and metastasis. Am J Pathol. 2010;177(3):1053–64.
- 6. Vasiley SA., Lentz S. AA. Gynecologic Oncology. Wiley Blackwell. 2011.
- 7. Debashis D. Ovarian Cancer The Silent Killer. J Tumor Res. 2018;4(1): 1-5.
- Jonsen AR, Siegler M, Winslade WJ. Clinical ethics: a practical approach to ethical decisions in clinical medicine 7th ed. Mc Graw-Hill Med Publ Div. 2010:9– 225.
- 9. Berek JS, Hacker NF, Hengst T. Gynecologic Oncology. Sixth Edition. 2015: 658–86.
- 10. Smith JP. Surgery for ovarian cancer. Advances in the Biosciences. 2010; 26: 137–49.
- 11. Harsono AB. Kanker Ovarium : "The Silent Killer." Indones J Obstet Gynecol Sci. 2020;3(1):1–6.
- 12. Di Saia PJ, Creasman WT. Clinical Gynecologic Oncology. 9th ed. Clin Gynecol Oncol Can. Elsevier. 2018.
- Hopkins TG, Stavraka C, Gabra H, Fallowfield L, Hood C, Blagden S. Sexual activity and functioning in ovarian cancer survivors: An internet-based evaluation. Climacteric. 2015;18(1):94–8.

- Teng FF, Kalloger SE, Brotto L, Mc.Alpine JN. Determination of quality of life in ovarian cancer survivors. A pilot study. J Obstet Gynecol Can. 2014;36(8): 708-15.
- Ginting KB, Yaznil MR, Prabudi MO, Rahmawati L. Quality of life among ovarian cancer survivors in Haji Adam Malik General Hospital Medan. Indonesia. Heal Sci J Indones. 2020;11(2):133–9.
- Afandi D. Kaidah dasar bioetika dalam pengambilan keputusan klinis yang etis. Maj Ked Andalas. 2017;40(2):111.
- 17. Afandi D. Aspek medikolegal dan tata laksana persetujuan tindakan kedokteran. J Kes Melayu. 2018;1(2):99–105.
- Mappaware NA, Sima S, Syahril E, Mokhtar S, Royani I, Mursyid M. Stage III-B cervical-cancer of young age in medical, bioethics, and clinical ethics perspectives. Indian J Forens Med Toxicol. 2020; 14(2): 2565-70.
- 19. Gillon R. Defending the four principles approach as a good basis for good medical practice and therefore for good medical ethics. J Med Ethics. 2015; 41: 111-6.
- 20. Green DS, Ercolano E, Dowd M, Schwartz PMR. Quality of life among women after surgery for ovarian cancer. Palliat Support Care. 2008;6(3):239–47.
- 21. Purwadianto A. The contextual aspect of prima facie selection of ethical dilemma cases and the resolution of concrete ethical cases. Non degree program in Bioethics, Medical Law and Human Rights. HWS Dikti. Jakarta. 2007: 1-7.