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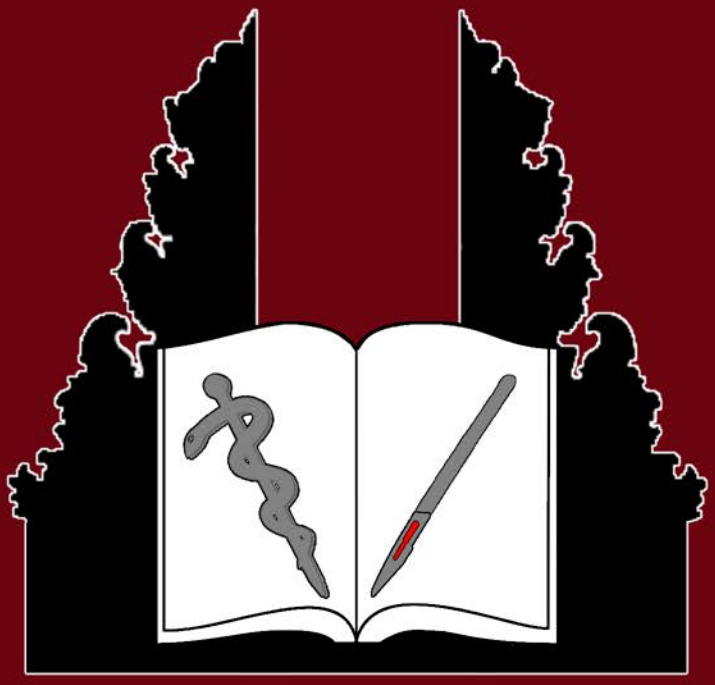

The Relationship between Obesity, Intraoperative Blood Loss, NLR, and CRP with Perioperative Complications in Colorectal Cancer Surgery

Low Immunoscores CD3/CD8 and CD3/CD45RO are Associated with The Low Survival Rate of Triple Negative Breast Cancer Patients

Meckel's Diverticulitis Causing Acute Intestinal Obstruction In Rural Area: A Rare Case Report

Kikuchi Disease of Parotid Gland

Simultaneous Extended Right Hemicolectomy and Anterior Resection for Synchronous Colon Cancer: A Case Report

Thyroid Malignancy in Clinically Benign Cystic Thyroid Nodule Presentation

Studi Analisis dan *Literature Review* Tentang Perbandingan *Glasgow Outcome Scale-Extended (GOS-E)* dan *Disability Rating Scale (DRS)* dalam Penilaian Hasil Cedera Otak Traumatik

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Pedoman untuk penulis

Majalah ilmiah JBN (Jurnal Bedah Nasional) menerima sumbangan naskah yang berhubungan dengan ilmu bedah dari para dokter dan ilmuwan di seluruh Indonesia, baik berupa karangan asli, ikhtisar pustaka, laporan kasus, maupun surat untuk redaksi. Naskah yang dikirimkan untuk majalah Jurnal Bedah Nasional adalah naskah belum pernah atau tidak akan dikirim ke majalah lain. Bahasa yang digunakan adalah Bahasa Indonesia atau Inggris.

Ejaan yang dipakai hendaknya sesuai dengan ejaan pada Kamus Besar Bahasa Indonesia. Jika naskah dalam bahasa Inggris, hendaknya memakai pedoman ejaan *the Oxford English Dictionary* atau *Webster Dictionary*.

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Abstrak harus ditulis dalam Bahasa Indonesia dan Inggris sebanyak maksimal 250 kata dan disertai dengan 3 sampai 5 kata kunci. Abstrak ditulis dalam format satu paragraf.

Artikel (*Original Article*) bersifat ilmiah dan informatif, disusun sepadat dan sejelas mungkin. Setelah judul, isi karangan asli disusun dalam urutan sebagai berikut: i) Abstrak, ii) Pendahuluan, iii) Bahan dan Metode, iv) Hasil, v) Pembahasan, dan vi) Simpulan dan Saran, vii) Pernyataan terima kasih (kalau ada), viii) Daftar Pustaka (berisi 10 tahun terakhir).

Ihktisar pustaka (*Review Article*) sebaiknya berisikan masalah yang sedang hangat dan isinya akan memberikan pencerahan serta memperluas atau memperdalam wawasan ilmiah pembaca tentang topic bahasan. Setelah judul, ikhtisar pustaka disusun dalam urutan sebagai berikut: i) Abstrak, ii) Pendahuluan (maksimal 1 halaman), iii) Sub-judul menunjukkan gagasan dasar, iv) Ringkasan, v) Daftar Pustaka (berisi 10 tahun terakhir).

Laporan kasus (*Case Report*), setelah judul sebaiknya disusun dalam urutan sebagai berikut: i) Abstrak, ii) Pendahuluan (maksimal 1 halaman), iii) Ilustrasi kasus, iv) Diskusi, v) Ringkasan, vi) Daftar Pustaka (10 tahun terakhir).

Ilustrasi yang menyertai naskah berupa gambar, tabel atau grafik. Penggunaan ilustrasi dibatasi pada hal-hal yang relevan dengan isi naskah. Tabel harus dapat berfungsi sendiri tanpa memerlukan tambahan keterangan dari naskah. Tabel memuat bagian-bagiannya, yaitu: a) nomor tabel, b) judul tabel, c) keterangan, dan d) data-data dalam angka. Skala grafik dipilih dengan seksama.

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ORIGINAL ARTICLE
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The Relationship between Obesity, Intraoperative Blood Loss, NLR, and CRP with Perioperative Complications in Colorectal Cancer Surgery

Lambertus Josef F. Buga[1*], Gede Eka Rusdi Antara[2], Made Agus Dwianthara Sueta[2], I Made Mulyawan[2], Ida Bagus Made Suryawisesa[3], Ida Bagus Budiarta[4]

[1]General Surgery Training Programme, Faculty of Medicine, Udayana University/Prof. Dr. I.G.N.G Ngoerah General Hospital, Denpasar, Bali, Indonesia.
[2] Digestive Surgery Department, Faculty of Medicine, Udayana University/Prof. Dr. I.G.N.G Ngoerah General Hospital, Denpasar, Bali, Indonesia.
[3] Oncology Surgery Department, Faculty of Medicine, Udayana University/Prof. Dr. I.G.N.G Ngoerah General Hospital, Denpasar, Bali, Indonesia.
[4] Vascular Surgery Department, Faculty of Medicine, Udayana University/Prof. Dr. I.G.N.G Ngoerah General Hospital, Denpasar, Bali, Indonesia.

*Correspondence author: yosephbuga@gmail.com.

ABSTRACT

Aim: This study examines the relationship between obesity, intraoperative blood loss, and systemic inflammatory responses (NLR and CRP) concerning perioperative complications in colorectal cancer surgery. **Methods:** A retrospective analytical observational study was conducted on 96 patients who underwent colorectal cancer surgery from January 1 to August 31, 2023. The analysis included obesity history, intraoperative blood loss, NLR, and CRP levels, using descriptive statistics, Chi-Square tests for Odds Ratios (OR), and logistic regression for adjusted odds ratios. **Results:** The study found a 38.5% complication rate in patients with BMI ≥25 kg/m² (OR=35) and a 29.5% rate in those with CRP >150 mg/L (OR=7). Patients with NLR >3 had a 21.1% complication rate (OR=1.3), while those with intraoperative blood loss >800 mL faced an 83.3% complication rate (OR=36). Logistic regression indicated that obesity and CRP are independently associated with major complications. **Conclusion:** Obesity, intraoperative blood loss, NLR, and CRP collectively influence major perioperative complications, with obesity and CRP being the most significant independent factors in colorectal cancer surgery.

Keywords: Colorectal cancer, obesity, CRP, NLR, intraoperative blood loss, major perioperative, complications.

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INTRODUCTION

Colorectal cancer (CRC) is a malignant tumor that arises from the epithelial tissue of the colon and rectum.[1] CRC is a highly heterogeneous malignancy caused by the interaction between genetic and environmental factors. The incidence of CRC is approximately 1.2 million each year worldwide. CRC is the second most common malignancy in women (614,000 cases/year) and the third most common in men (746,000 cases/year).[2]

According to the American Cancer Society, CRC is the third most commonly diagnosed cancer and also the third leading cause of cancer-related mortality in both men and women.[3] In Indonesia, CRC ranks as the third most prevalent cancer and has shown a significant increase in incidence, about 12.8 per 100,000 adults, with a mortality rate of 9.5% of all cancer cases.[4] The incidence in men is comparable to women and tends to occur more frequent in the productive age group. In contrast, data from Western countries reported that CRC is mostly diagnosed in elderly patients.[3]

A study by Gunasekaran et al.[5] reported 121 cases of CRC at Prof. I.G.N.G Ngoerah

General Hospital between 2013 and 2017. The highest number of cases occurred in the 50–60 years age group (39.7%), followed by the 61–70 years group (23.1%), while those aged over 70 had the lowest number (14.9%). Regarding gender, CRC was more prevalent in males (59.5%) than females (40.5%). The most common type was adenocarcinoma not otherwise specified (NOS) (97.5%) and diagnosed at stage II (53.7%).[5] Surgical resection is the best curative therapy for CRC. However, it carries a high risk of recurrence. Furthermore, CRC surgery is not free of postoperative morbidity and mortality concerns.[2]

This study aims to investigate the association between obesity, intraoperative blood loss in colorectal cancer surgery, and systemic inflammatory response represented by neutrophil-to-lymphocyte ratio (NLR) and C-reactive protein (CRP) with the occurrence of major perioperative complications in colorectal cancer surgery.

METHODS

Retrospective observational analytic study was conducted at Prof. Dr. dr. I.G.N.G. Ngoerah General Hospital, Denpasar, Indonesia.

Subjects were selected using systematic random sampling. The inclusion criteria were as follows: (1) Patients aged ≥18 years who had been clinically diagnosed with colorectal cancer based on histopathological examination; (2) Patients with clinical staging of colorectal cancer classified as stage 0, I, IIa, IIb, IIc, IIIa, IIIb, IIIc, IVa, or IVb; (3) Patients who underwent surgical treatment including local excision/simple polypectomy, wide surgical resection with anastomosis, or resection of the primary tumor in cases of resectable metastatic disease, at Prof. Dr. dr. I.G.N.G. Ngoerah Hospital between January 1 and August 31, 2023.

The independent variables in this study included:

- Obesity, assessed based on body mass index (BMI), categorized as <25 kg/m² or ≥25 kg/m²;
- Intraoperative blood loss, categorized as ≤800 mL or >800 mL;
- Neutrophil-to-lymphocyte ratio (NLR), classified as low (≤3) or high (>3);
- C-reactive protein (CRP) level, categorized as ≤150 mg/L or >150 mg/L.

The dependent variable was the presence of major or minor perioperative complications related to colorectal cancer surgery. All study data were derived from electronic medical records system.

Descriptive analysis was conducted to summarize the characteristics of the study subjects. Comparative analysis was conducted using 2x2 cross-tabulations and the Chi-square (χ^2) test, reporting odds ratios (ORs) and 95% confidence intervals (CIs). Furthermore, logistic regression analysis was performed to evaluate the independent association between each variable and the occurrence of perioperative complications. This analysis reported adjusted odds ratios (aORs) with corresponding 95% CIs and p-values ($\alpha = 0.05$).

RESULTS

A total 96 subjects included to this study (**Table 1**). Most of the subjects were male (59.4%) with mean age was 54.82±10.845 years Patients with a body mass index (BMI) of <25 kg/m² (59.4%) were more prevalent than those with a BMI of ≥25 kg/m² (40.6%). Most patients have stage IVA (46.9%) and low grade (60.4%) tumor. The most frequently performed surgical procedures were wide surgical resection with anastomosis, resection of the primary tumor along with resectable metastases for colon cancer (38.5%) and

transabdominal resection for rectal cancer (33.3%).

Table 1. Characteristics of Subjects

Variable	Category	Frequency (N=96)	Percentage (%)
Sex	Male	57	59.4%
	Female	39	40.6%
Age	Mean ± SD	54.82 ± 10.845	–
Obesity (BMI)	<25 kg/m²	57	59.4%
	≥25 kg/m²	39	40.6%
Cancer Stage	I	1	1.0%
	IIA	10	10.4%
	IIIA	1	1.0%
	IIIB	19	19.8%
	IIIC	12	12.5%
	IVA	45	46.9%
	IVB	8	8.3%
Histopathological Grading	Well differentiated	6	6.3%
	Moderately differentiated / Low grade	58	60.4%
	Poorly differentiated / High grade	32	33.3%
Surgical Technique	Wide surgical resection + anastomosis, resection of primary tumor + resectable metastasis (colon cancer)	37	38.5%
	Transabdominal resection (AR or APR, LAR, TME) (rectal cancer)	32	33.3%
	Resection, stoma, or colonic stenting for unresectable metastatic tumors	27	28.1%
CRP Level	≤150 mg/L	52	54.2%
	>150 mg/L	44	45.8%
NLR	≤3	20	20.8%
	>3	76	79.2%
Intraoperative Blood Loss	≤800 mL	90	93.8%
	>800 mL	6	6.3%
Perioperative Complications	Minor	80	83.3%
	Major	16	16.7%

Regarding inflammatory markers and surgical outcomes, most patients had a CRP level of ≤150 mg/L (54.2%) and NLR values were predominantly high (>3) in 79.2% patients. A total of 90 patients (93.8%) experienced intraoperative blood loss ≤800 mL. Major complications occurred in (16.7%). The incidence of major perioperative complications was significantly higher among patients with a BMI ≥25 kg/m², CRP levels >150 mg/L, NLR >3, and intraoperative blood loss >800 mL (**Table 2**).

The results of multivariate analysis revealed that obesity (BMI ≥25 kg/m²) and elevated CRP levels were significantly associated with major complications.

DISCUSSION

In this study, most of the CRC patients were male. This finding is consistent with research conducted by Nikijuluw et al.[6] and Gunasekaran et al.[5] who reported a higher prevalence of CRC in males than females. The higher CRC incidence in males is associated with estradiol levels. Normal estradiol plays a

role in spermatogenesis and fertility; however, excessive estradiol inhibits gonadotropin secretion such as LH, which then reduces testosterone secretion. High testosterone levels are proven to be protective against CRC.[7] Additionally, alcohol consumption and smoking habits more common among men also trigger CRC. Excessive alcohol intake alters the normal condition of the gastrointestinal mucosa, promoted by the oxidation of acetaldehyde (a metabolite of ethanol), which promotes inflammation in the gastrointestinal tract mucosa and abnormal cell growth. Acetaldehyde also disrupts DNA repair by inhibiting enzymes involved in the process, binds with other molecules, and causes DNA mutations that can lead to carcinogenesis.[6]

Table 2. Comparison of Obesity, CRP, NLR, and Intraoperative Blood Loss and The Incidence of Perioperative Complications

Variable	Perioperative Complications		Bivariate Analysis			Multivariate Analysis		
	Minor (N=80)	Major (N=16)	OR	95% CI	P-value	Adjusted OR	95% CI	Adjusted p-value
Obesity (kg/m²)								
<25	56 (98.2%)	1 (1.8%)	35.000	4.373-280.140	0.000	21.665	2.558-183.475	0.005
≥25	24 (61.5%)	15 (38.5%)						
C-Reactive Protein (CRP) (mg/L)								
≤150	49 (94.2%)	3 (5.8%)	6.849	1.805-25.990	0.002	4.722	1.027-21.706	0.046
>150	31 (70.5%)	13 (29.5%)						
Neutrophil-Lymphocyte Ratio (NLR)								
≤3	20 (100%)	0 (0%)	1.267	1.128-1.432	0.025			
>3	60 (78.9%)	16 (21.1%)						
Intraoperative Blood Loss (mL)								
≤800	79 (87.8%)	11 (12.2%)	35.900	3.831-336.500	0.000	9.322	0.875-99.290	0.064
>800	1 (16.7%)	5 (83.3%)						

The average age of patient in this study was 54.82 ± 10.845 years, This finding is consistent with the American Cancer Society which states that the incidence of CRC is higher in individuals aged 50 years and older compared.[8] Similarly, Gunasekaran et al., in their study at Prof. Ngoerah General Hospital, found that the highest number of cases occurred in the 50–60 year age group.[5]

Colorectal cancer arises as the accumulation of various genetic and epigenetic alterations that transform normal epithelium into adenocarcinoma. Several causes include mutations in tumor suppressor genes such as APC, TP53, and DCC, as well as activating mutations in oncogenes like K-RAS. According to Sakai et al. in addition to mutations in tumor suppressor genes, aberrant DNA methylation also occurs, which can inactivate the signaling pathways of tumor suppressor genes. These aberrant methylation patterns and gene mutations increase with aging. Aging is associated with a decline in cellular and tissue function, impairing structural maintenance and repair processes, leading to the accumulation of cellular damage. Consequently, the body's overall resilience gradually diminishes, resulting in various metabolic distortions that give rise to degenerative and age-related diseases, such as CRC.[7]

Obesity (BMI ≥25 kg/m²) is a risk factor of major perioperative complication in CRC surgery. This finding aligns with research conducted by Chung et al. (2021), which showed that obesity increases the risk of postoperative complications in colorectal cancer patients undergoing surgery. Obesity-

induced dysregulation of the immune system, or obesity-related deficiencies in immune response-mediating cells, is a likely mechanism explaining the increased risk of complications.[9] Other study also support the conclusion that obesity increases the risk of perioperative complications, particularly major complications.[10]

In this study, intraoperative blood loss (IBL)>800 mL was not an independent risk factor of major perioperative complications in CRC surgery. There is still a lack of research explaining the association between intraoperative blood loss and the occurrence of perioperative complications in CRC surgery. Tamagawa et al.[11] in their study analyzing data from over 1,500 cases, reported that IBL ≥200 mL was an independent risk factor for poor overall survival (OS), disease-free survival (DFS), and postoperative morbidity in stage II/III CRC patients undergoing radical surgery. In the TNM classification, T-stage affects the amount of blood loss, as surgery for advanced T-stage cancer likely requires more extensive dissection.[11]

Intraoperative blood loss (IBL) induce suppression in the activity or cytotoxicity of natural killer (NK) cells. This reduction correlates with the volume of blood loss. Several studies have found that perioperative blood transfusions can also suppress immune function and increase the risk of recurrence and metastasis. Perioperative transfusions resulting from blood loss can accelerate tumor progression by inducing inflammatory responses and immunosuppression. Allogeneic blood products release inflammatory factors during storage and can lead to immunosuppression, including inhibition of NK cell activity and reduction in the Th1/Th2 ratio, thereby increasing the risk of infectious complications after transfusion.[12]

Systemic inflammatory responses play a role in the development of various cancers through genetic mutations, genomic instability, epigenetic modifications, cancer cell proliferation at different stages, and tumor metastasis. Macrophages are abundant in the lamina propria of the intestine, and tumor-associated macrophages (TAMs) are linked to tumor progression. Type I macrophages (M1) produce pro-inflammatory cytokines involved in pathogen defense and tumor cell killing mechanisms, such as tumor necrosis factor-α (TNF-α), interleukin-12 (IL-12), and create an oxidative environment through the production of inducible nitric oxide synthase (iNOS) and reactive oxygen species (ROS). Type I macrophages also produce IL-23, which stimulates IL-17. IL-17 in turn induces the production of IL-1, IL-6, IL-8, chemokine ligand 1, and TNF-α in stromal, epithelial, endothelial cells, and monocyte subsets. These pro-inflammatory cytokines collectively recruit neutrophils to peripheral tissues for phagocytosis and apoptosis. Neutrophil apoptosis reduces IL-23 secretion and thus decreases IL-17, granulocyte-colony stimulating factor (G-CSF), and granulopoiesis. In chronic inflammatory conditions such as colorectal cancer, this process is disrupted. IL-23 continues to be produced, promoting IL-17 expression and increasing the presence of neutrophils and monocytes in peripheral tissues. These changes result in the accumulation of neutrophils during chronic inflammation, which promotes tumor growth. Unremoved apoptotic neutrophils release intracellular granules that cause further tissue damage. This explains why NLR levels tend to be elevated in patients with colorectal cancer.[16,19,23]

Putera et al.[19] in their study, explained that a high NLR is associated with more advanced stages of colorectal cancer. In this study, high NLR increase the risk of major complication, although it is not considered an independent factor. The finding of a significant association

between NLR and perioperative complications in CRC surgery supports the role of NLR as a prognostic marker in assessing the risk of perioperative complications.

C-reactive protein (CRP) level was associated the occurrence of major perioperative complications in this study. This finding is consistent with studies by Lee *et al.* and Nisa which explained that higher CRP levels were associated with an increased risk of cancer recurrence and mortality from colorectal cancer in patients undergoing surgery.[13,22] McSorley et al. also suggested CRP threshold values of 190 mg/L on postoperative day (POD) 2, 170 mg/L on POD 3, and 145 mg/L on POD 4. They recommended that CRP concentrations above the 150 mg/L between POD 3–5 should prompt immediate investigation and/or management of potential postoperative complications in CRC surgery.[14]

Inflammatory pathways can contribute to tumor development by enhancing cell movement, increasing blood vessel permeability, and stimulating the formation of new blood vessels. Cancer cells may secrete various cytokines and chemokines, attracting inflammatory cells into the tumor microenvironment (TME) and elevating levels of C-reactive protein (CRP) in the bloodstream. CRP can attach to the surface of dying cells and trigger the classical complement pathway, promoting the tagging and removal of these cells by phagocytes. It also has the ability to attract C4b-binding protein, an important inhibitor of the classical complement pathway, and influence the function of immune cells like macrophages, neutrophils, and monocytes. As such, CRP functions not only as a marker of inflammation but also plays a role in regulating innate immune responses.[24]

CONCLUSION

Obesity, intraoperative blood loss, NLR, and CRP are simultaneously associated with the occurrence of major perioperative complications. However, only obesity and CRP are identified as independent factors with major perioperative complications in CRC surgery.

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DISCLOSURE

The author stated that there was no conflict of interest in any form in the preparation of this research article.

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ORIGINAL ARTICLE
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Low Immunoscores CD3/CD8 and CD3/CD45RO are Associated with The Low Survival Rate of Triple Negative Breast Cancer Patients

Stacia Novia Marta[1*], Ni Gusti Ayu Agung Manik Yuniawaty Wetan[2], Ida Bagus Made Suryawisesa[2], Putu Anda Tusta Adiputra[2]

[1]Department of surgery, Faculty of Medicine, Universitas Udayana, Prof. Dr. dr. I.G.N.G Ngoerah, Denpasar, Bali.
[2]Division of surgical oncology, Department of surgery, Faculty of Medicine, Universitas Udayana, Prof. Dr. dr. I.G.N.G Ngoerah, Denpasar, Bali.

*Corresponding author: stacianoviamarta@gmail.com.

ABSTRACT

Aim: Triple-negative breast cancer (TNBC) is associated with a highly aggressive clinical course, contributing to poorer patient outcomes and higher mortality rates. Current prognostic tools do not fully capture the complexities of the tumor immune microenvironment, particularly the role of effector lymphocytes (CD3, CD8, and CD45RO). Therefore, this study was conducted to investigate the prognostic significance of the immune markers CD3, CD8, and CD45RO within the tumor microenvironment of TNBC patients. **Methods:** This retrospective cohort study involved women aged >18 years old diagnosed with TNBC. Immunohistochemistry (IHC) for CD3, CD8, and CD45RO was performed using the Novolink system. Two pathologists independently assessed cell density in the tumor center (CT) and invasive margin (IM). Densities were classified as high or low using ROC curves, and the immunoscores (CD3/CD8, CD3/CD45RO) were grouped into low (I0, I1) and high (I2, I3, I4). Two-year mortality and clinical data were collected from medical records. Survival rates were analyzed using Kaplan-Meier and compared with the log-rank test. **Results:** The 2-year survival rate for TNBC patients was 58.3%, with a mean survival time of 18.95 months. Low CD3/CD8 was associated with significantly lower survival compared to high CD3/CD8 (42.9% vs. 73%; p=0.013), with mean survival times of 17.03 vs. 20.80 months. Similarly, low CD3/CD45RO had lower survival than high CD3/CD45RO (38.5% vs. 69.6%; p=0.01), with mean survival times of 16.37 vs. 20.43 months. **Conclusion:** Low CD3/CD8 and CD3/CD45RO immunoscores are associated with low survival in TNBC patients.

Keywords: CD3/CD8 immunoscore, CD3/CD45RO immunoscore, survival, triple negative breast cancer.

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INTRODUCTION

Breast cancer is one of the most common cancer in women with a high mortality rate. Globocan data in 2020 showed that about 2.2 million new cases of breast cancer were diagnosed globally[1], which represents around 11.7% of all cancer cases. As many as 24% of all breast cancer cases in the world were reported in Asia Pacific with an incidence rate of 30 cases per 100,000 population. Indonesia ranks third in Asia by accounting for 12% of breast cancer cases.[2]

Triple negative breast cancer (TNBC) is a subtype of breast cancer with no expression of estrogen, progesterone, and human epidermal receptor-2 (HER-2). This subtype not only has more aggressive characteristics than the others but also has a poorer prognosis.[3] This is also supported by the theory that TNBC is the most immunogenic breast cancer with the fastest evolving and adapting capability.[4] There are several studies which designed predictive models for survival of TNBC, including clinicopathological criteria and the American

Joint Committee on Cancer (AJCC) TNM. However, the diagnostic values of these model were less significant.[5]

A more specific prognosis predictor system based on immunity profile is needed, especially to predict mortality of TNBC patients. The immune profile of the cancer microenvironment is an important factor to progressivity and prognosis of TNBC through increased effectiveness of chemotherapy. In TBNC cases, hormonal therapies and HER2-targeted treatments tends to be unresponsive due to the absence of estrogen receptors, progesterone receptors, and HER2 amplification.[6]

Tumor immune microenvironment plays a critical role in the progression and treatment response of TNBC. Within the tumor environment, neutrophils (as well-recognized important regulators of cancer progression) impact the immune response by switching between pro-tumor and anti-tumor activities. Other leukocyte types then gather neoantigens from the destroyed cancer cells, triggering an immune response against the tumor. These immune cells work together in a complex way to influence cancer development and patient prognosis.[6] One type of leukocyte, lymphocyte, has become a strong candidate in the development of TNBC mortality predictor models.[4]

Effector lymphocytes can be identified by three key CD markers: CD3 (a general lymphocyte marker), CD8 (cytotoxic T-lymphocytes), and CD45RO (memory T-cells). The combination of CD3/CD8 and CD3/CD45RO is commonly referred to as the immunoscore. In particular, tumor-infiltrating lymphocytes (TILs), including CD3+ T cells, CD8+ cytotoxic T cells, and memory T cells marked by CD45RO, are important indicators of the immune response against the tumor. Higher levels of these lymphocytes, especially CD8+ T cells, have been associated with better clinical outcomes, as they contribute to the immune system's ability to recognize and eliminate cancer cells. Evaluating the presence and activity of lymphocytes in TNBC tumors may help guide prognosis and therapeutic strategies, as immunotherapy emerges as a promising approach for treating this challenging cancer.[6]

Even though several biomarkers have been reported to help clinician to making prognosis and determining the potential treatment modalities for TNBC cases. Unfortunately, currently available prognostic tools do not fully capture the complexities of the tumor immune microenvironment, particularly the role of effector lymphocytes (CD3, CD8, and CD45RO), and there were only limited information regarding this issue. This creates an urgent need to explore alternative prognostic tools, such as the role of the immune system in TNBC progression. Given the potential benefits of utilizing immunoscores in TNBC, further research is essential to investigate how CD3/CD8 and CD3/CD45RO immunoscores might impact the survival of TNBC patients. Therefore, this study was conducted to address this gap and evaluate the prognostic value of these markers in TNBC patients' survival.

METHODS

This retrospective cohort study was conducted to evaluate the survival of TNBC patients receiving neoadjuvant chemotherapy, based on CD3/CD8 and CD3/CD45RO immunoscores. The study was carried out at Prof. Dr. I.G.N.G. Ngoerah Denpasar General Hospital and Prima Medika Private Hospital in Denpasar, Bali. Subjects were observed from diagnosis for up to 24 months, with data collected from medical records and the Indonesian Surgical Oncology Society cancer registry. The recruitment period spanned from

January 2020 to January 2022, while subject observation was conducted from 2022 to 2024.

The study included women aged >18 years old who were diagnosed with TNBC based on histopathological and immunohistochemical examinations, had received neoadjuvant chemotherapy, and had paraffin blocks that was readable and not defective. Subjects with relapse cases, a history of other malignancies, immunodeficiency disorders, and death caused by other diseases were excluded from the study. The protocol of this study was approved by the Ethics Committee of the Faculty of Medicine, Universitas Udayana (No. 1045/UNI4.2.2.VII.14/LT/2023).

The tumor samples from both the tumor center (CT) and invasive margin (IM) were processed for immunohistochemical examinations using primary antibodies against CD3 (catalogue number: [PA0553], monoclonal, mouse), CD8 (catalogue number: [PA0183], monoclonal, mouse), and CD45RO (catalogue number: [PA0146], polyclonal, rabbit) based on the Novolink Min Polymer Detection system (Novacastra, Leica Biosystem Newcastle Ltd, UK). Chromogen DAB (3,3'-diaminobenzidine tetrahydrochloride) was applied to the specimens, followed by staining with hematoxylin.

Density evaluation of CD3, CD8, and CD45RO on CT and IM was performed independently by two certified pathologists at 40x magnification. The area for density measurement was selected based on the most representative regions of the tumor as identified by the pathologists. For this, the double-blind process involved the pathologist collecting data without knowledge of the subjects' outcome (whether they survived or not). The selected spots were then photographed using a lens connected to the microscope. From these photographs, the analysis was performed and the density was quantified by counting the number of cells per mm^2.

The data was provided as a single dataset from the pathology lab of Prof. Dr. I.G.N.G. Ngoerah Denpasar General Hospital, as the hospital issues one result per examination. A ROC curve was used to classify CD3, CD8, and CD45RO densities in CT and IM as high or low. The cut-off values used for categorizing immunoscores into high and low groups were defined as follows: CD3 in the CT at 16.5 cells/mm^2, CD3 in the IM at 41 cells/mm^2, CD8 in the CT at

15.5 cells/mm^2, CD8 in the IM at 24.5 cells/mm^2, CD45RO in the CT at 30.5 cells/mm^2, and CD45RO in the IM at 23 cells/mm^2. The optimal cut-off value was determined using the Youden Index, and sensitivity, specificity, area under the curve (AUC), and 95% confidence interval (95% CI) values were reported (Table 1). Immunoscores for CD3/CD8 and CD3/CD45RO were classified into two groups: low values (I0 and I1) and high values (I2, I3, and I4). To ensure accuracy and minimize bias, both pathologists underwent certification and were blinded to the clinical outcomes during their evaluations, and it was confirmed that the hospital laboratory is certified and standardized for CD3, CD8, and CD45RO measurements

The assessment of 2-year mortality status was conducted based on medical record. The mortality data was collected from the subjects' medical records during their last visit to the clinic or hospital. This data included death certificates, and in some cases, coordination was done by contacting the subjects' family by phone to confirm whether the patient was still alive or had passed away.

Other data such as age, menopausal status, number of parities, stage, tumor size, lymph node spread, distant metastases, histopathologic type, grade, TIL and

lymphovascular invasion (LVI) were also collected from medical records.

All statistical analysis processes were carried out with the Statistical Package for Social Science (SPSS) program. In this study, data analysis consisted of univariate, bivariate, and multivariate analysis. Descriptive analysis was conducted to describe the characteristics data of TNBC patient. Kaplan-Meier analysis was used to calculate survival rate. The comparison of survival rate was calculated using log-rank test.

The cox proportional hazard regression test aimed to assess the association (adjusted) of each independent variable to the survival of TNBC patients by controlling for confounding variables. Hazard Ratio was presented as a measurement of risk. The inference process was initiated with a confidence level of 95% and a value of $p<0.05$.

RESULTS

This study included 72 TNBC patients, with 30 dying and 42 surviving over a 2-year survival period. There were no significant differences in age, parity, menopausal status, tumor size, lymph node involvement, distant metastases, histopathologic type, grade, TIL, LVI based on mortality status within 2 years ($p>0.05$). The basic characteristics of the sample were presented in **Table 1**. Additionally, the immunoscore was calculated by comparing intratumoral and tumor margin samples. However, no data on significant differences in immunoscore between these two populations is presented in this study. For future research, it would be valuable to assess whether there are significant differences in immunoscore between intratumoral and tumor margin samples to improve sampling strategies and better understand the tumor's immune environment.

Table 1. Characteristics of Research Sample.

Variables	Mortality		P value
	Died (N=30)	Alive (N=42)	
Age			0.732
≥40 years	25 (83.3%)	37 (88.1%)	
<40 years	5 (16.7%)	5 (11.9%)	
Parity			0.214
1-3	13 (43.3%)	10 (23.8%)	
>3	13 (43.3%)	25 (59.5%)	
Missing data	4 (13.3%)	7 (16.7%)	
Menopause			0.513
Pre-menopause	17 (56.7%)	27 (64.3%)	
Post-menopause	13 (43.3%)	15 (35.7%)	
Tumor size (T)			1.000
T1-T2	3 (10%)	5 (11.9%)	
T3-T4	27 (90%)	37 (88.1%)	
Lymph node involvement (N)			1.000
N0	2 (6.7%)	3 (7.1%)	
N1-2	28 (93.3%)	39 (92.9%)	
Distant metastasis (M)			0.848
M0	23 (76.7%)	33 (78.6%)	
M1	7 (23.3%)	9 (21.4%)	
Histopathological type			0.288
NST	28 (93.3%)	35 (83.3%)	
Others	2 (6.7%)	7 (16.7%)	

Grade			0.765
Low (1-2)	9 (30%)	14 (33.3%)	
High (3)	21 (70%)	28 (66.7%)	
TIL			0.814
Positive	26 (86.7%)	34 (81%)	
Negative	2 (6.7%)	4 (9.5%)	
Missing data	2 (6.7%)	4 (9.5%)	
LVI			0.214
Positive	13 (43.3%)	10 (23.8%)	
Negative	13 (43.3%)	25 (59.5%)	
Missing data	4 (13.3%)	7 (16.7%)	

The 2-years overall survival (OS) of TNBC patients in this study was 58.3%. The mean survival time was 18.95 months. The low immunoscore CD3/CD8 group had a significantly lower 2-year survival than the high immunoscore CD3/CD8 group (42.9% vs. 73%; p=0.013).

The mean survival time of the high immunoscore CD3/CD8 group was 20.80 months and the low immunoscore CD3/CD8 group was 17.03 months (Figure 1). The low immunoscore CD3/CD45RO group also had significantly lower 2-year survival than the the high immunoscore CD3/CD45RO group (38.5% vs 69.6%; p=0.01). The mean survival time in the high immunoscore CD3/CD45RO group was 20.43 months, while in the low immunoscore CD3/CD45RO group it was 16.37 months (**Figure 1**).

Figures 3 and **Figure 4** illustrate the density evaluation of CD3-positive cells under 40x magnification, with red arrows indicating stained cells. These figures demonstrate the histological differences in CD3-positive cell infiltration, which were quantified to determine the immunoscores used in the survival analyses.

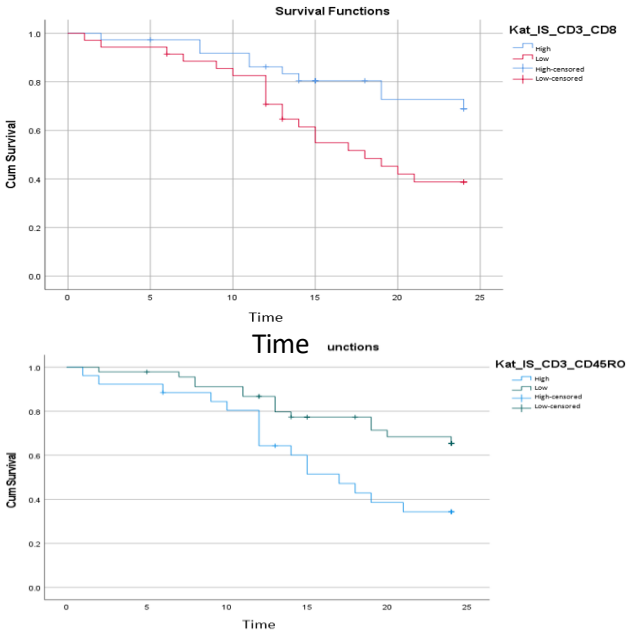

Figure 1. Kaplan Meier Survival Curve Based on Immunoscore CD3/CD8 and CD3/CD45RO

Table 2. Immunoscore CD3/CD8 and CD3/CD45RO Based on 2-Years Mortality.

Variable	2-Years Mortality		P value
	Died (N=30)	Alive (N=42)	
Immunoscore CD3/CD8			0.01
Low	20 (66.7%)	15 (35.7%)	
High	10 (33.3%)	27 (64.3%)	
Immunoscore CD3/CD45RO			0.01
Low	16 (53.3%)	10 (23.8%)	
High	14 (46.7%)	32 (76.2%)	

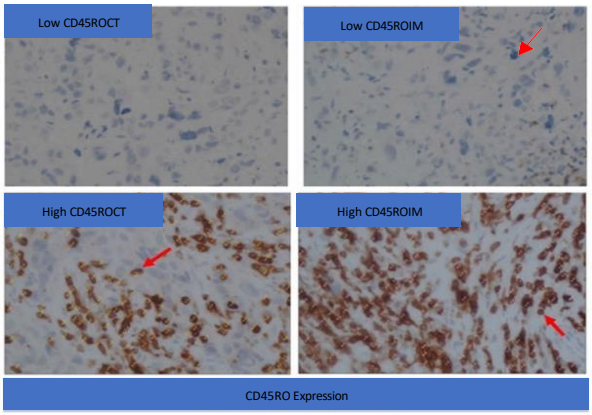

Figure 2. Density evaluation of CD45RO at 40x magnification. The red arrow indicates stained cells.

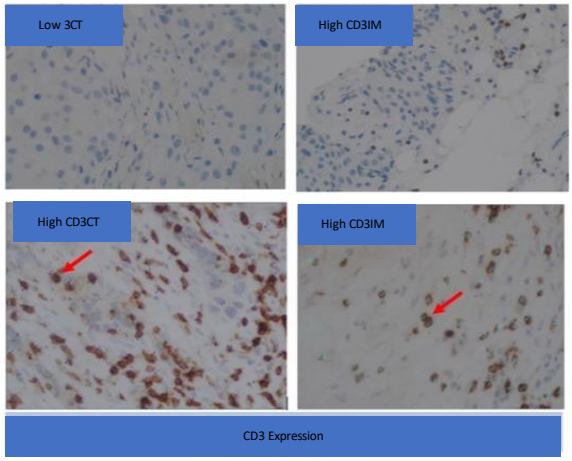

Figure 3. Density evaluation of CD3 at 40x magnification. The red arrow indicates stained cells.

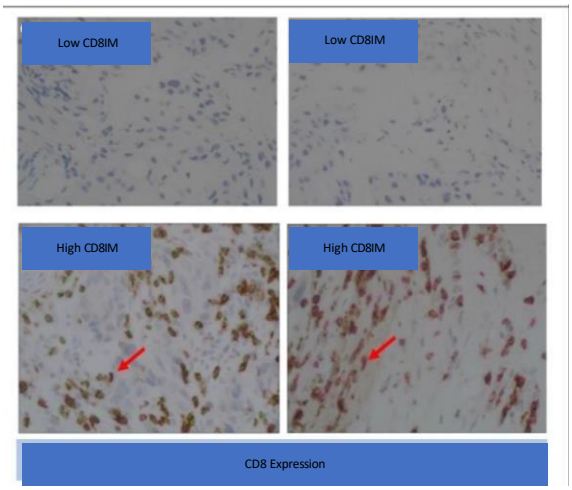

Figure 4. Density evaluation of CD3 at 40x magnification. The red arrow indicates stained cells.

Bivariate analysis revealed the significant association between CD3/CD8 and CD3/CD45RO immunoscores and 2-year mortality of patients (**Table 2**).

We cannot perform further statistical analysis by classifying the 72 subjects based on combinations of Low CD3/CD8, High CD3/CD8, Low CD3/CD45RO, and High CD3/CD45RO, and then determining whether those subjects were alive or deceased within 2 years, cannot be fulfilled due to the small sample size in the mortality group (n=30). Conducting this classification with such a limited number of subjects would yield insufficient data for meaningful statistical analysis. Additionally, the suggestion to perform similar analysis for Table 2 by separating the dead (n=30) and alive (n=42) subjects based on clinical variables faces the same limitation. Instead, we have relied on the existing tables and analyses, which provide a more comprehensive and statistically valid representation of the data. This ensures that the findings remain reliable without over-fragmenting the sample.

DISCUSSION

Triple Negative Breast Cancer (TNBC) is characterized by the absence of estrogen receptors (ER), progesterone receptors (PR), and HER-2 receptors, making it resistant to hormonal and HER-2 targeted therapies.[11] In this study, survival rate in TNBC patients was lower than in previous studies. A study with 133 months of follow-up noted 30.9% mortality and 38% disease progression.[12] Another found 5-year overall survival (OS) and disease-free survival (DFS) rates of 73.7% and 67%, respectively, with age, tumor size, and lymph node involvement significantly affecting outcomes.[13]

CD8 T cells are key players in the tumor-infiltrating lymphocyte (TIL) population and tumor immune microenvironment (TIME).

They act as cytotoxic cells, directly killing cancer cells, while CD4 T cells regulate their function. TNBC tumors have higher CD8 expression, which correlates with increased interferon (IFN)-γ responses and enhanced anti-tumor immune activity. IFN-γ also induces apoptosis, inhibits angiogenesis, and activates macrophages.[14,15,16] CD8 T cells eliminate tumor cells through granule release—containing granzyme, perforin, and granulysin—that penetrate target cell membranes, either via direct fusion or endocytosis. Additionally, they express Fas ligand (FASL), which activates apoptosis by engaging with Fas receptors on target cells, leading to caspase activation and DNA fragmentation.[16,17]

In addition to CD8, CD3 T cells are also directly related to tumor microinvasion status.4,18 This study observed that patients with low CD3/CD8 immunoscores had worse 2- year survival compared to those with high immunoscores, contrasting with earlier studies where immunoscores showed no significant correlation with survival. A limited sample size, especially in stages IIB and III, might explain these discrepancies.[19] Higher pathological complete response (pCR) rates were observed in patients with high CD3/CD8 immunoscores, reinforcing their prognostic value.[20]

CD45RO memory T cells are another crucial component of TIL.[21] They help generate long-term immune memory after antigen recognition by converting naïve CD45RA T cells into mature CD45RO T cells. These memory cells can be classified into central memory (Tcm) and effector memory (Tem) cells, with Tcm migrating to lymph nodes and Tem remaining in tumor sites for immediate response.[22,23,24] When cancer antigens are detected, these Tem cells can immediately perform effector functions to kill tumor cells without the need for further differentiation. Conversely, Tcm cells lack of effector function, therefore it differrentiate immediately into Tem cells after restimulation by antigens.[25] This mechanism confirms that the role of CD45RO memory T cells is highly dependent on CD8 T cells as effector cells.

In this study, patients with low CD3/CD45RO immunoscores had worse 2-year survival compared to those with high scores, consistent with prior research linking higher CD45RO density to better OS and DFS.[25,26] High expression of CD45RO has been associated with improved immune responses, reducing the likelihood of residual tumors or metastases.[27] However, CD45RO density is not universally predictive. For example, in renal cell carcinoma (RCC), higher CD45RO density correlated with poorer prognosis, likely due to dysfunctional TILs unable to mount effective anti-tumor responses.[27,29]

This study faced several limitations. Incomplete data introduced potential bias, as missing data were not excluded to preserve sample size. Manual calculation of CD3, CD8, and CD45RO densities—despite efforts to minimize discrepancies—may have introduced variability. Additionally, the lack of sufficient follow-up prevented the evaluation of DFS and RFS. Future research should address these limitations by increasing sample sizes and conducting multi-center collaborations. Automated immune cell quantification techniques would improve accuracy, reducing bias. Longitudinal studies are needed to better assess survival outcomes and understand the role of TILs, especially CD8+ T cells. Exploring immune checkpoint inhibitors could also provide insights into novel therapeutic strategies for TNBC.

CONCLUSION

Low CD3/CD8 was associated with significantly lower survival compared to high

CD3/CD8. Similarly, low CD3/CD45RO had lower survival than high CD3/CD45RO. This study proves that immunoscores CD3/CD8 and CD3/CD45RO can predict the survival in TNBC patients.

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DISCLOSURE

The author stated that there was no conflict of interest. SVM, IBS, and PATA were involved in concepting and planning the research, SVM performed the data acquisition/collection, calculated the experimental data and performed the analysis. SVM and IGBS drafted the manuscript and designed the figures, interpreting the results. IBS, PATA, IGBS, took parts in giving critical revision of the manuscript.

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CASE REPORT

Meckel's Diverticulitis Causing Acute Intestinal Obstruction in Rural Area: a Rare Case Report

Hendrik[1]*, I Gede Made Dwi Arya Pramaharta[2]

[1]General Practitioner, Regional Public Hospital (RSUD) Lewoleba, Lembata Regency, East Nusa Tenggara, Indonesia
[2]General Surgery Resident, Faculty of Medicine, Udayana University, Bali, Indonesia

*Corresponding author: iniemailhendrik80@gmail.com.

ABSTRACT

Aim: To study acute intestinal obstruction as complication of Meckel's diverticulitis in rural area. **Case Presentation:** A 13-year-old boy presented with diffuse abdominal pain, nausea, vomiting, and abdominal distension persisting for four days. The abdominal X-ray revealed dilated bowel loops and air-fluid levels, indicating obstruction. During exploratory laparotomy, a mesodiverticular band compressing the ileum was identified, along with a perforated Meckel's diverticulum approximately 100 cm proximal to the ileocecal junction. The trapped intestinal loop was released, and the diverticulum was resected. The procedure included peritoneal lavage and drain placement. The patient was closely monitored postoperatively, with further management tailored according to clinical progress and histopathological findings. **Conclusion:** This case underscores the importance of early diagnosis and individualized surgical strategies in complicated Meckel's diverticulum, particularly in resource-limited settings. Open laparotomy remains the preferred method for severe cases involving perforation or obstruction

Keywords: abdominal pain, intestinal obstruction, laparotomy, meckel's diverticulum, pediatrics.

DOI: https://doi.org/10.24843/JBN.2025.v09.i02.p03

INTRODUCTION

Meckel's diverticulum, a congenital pouch resulting from incomplete obliteration of the vitelline duct, affects 1-3% of the population. Although most cases are asymptomatic, complications such as diverticulitis, bleeding, and obstruction can occur. Meckel's diverticulitis, in particular, presents with symptoms mimicking acute appendicitis, including abdominal pain and tenderness, complicating early diagnosis.[1,2] The condition can lead to intestinal obstruction, often due to mesodiverticular bands trapping intestinal loops, or perforation from ectopic gastric tissue secreting acid. Such cases may necessitate prompt surgical intervention to avoid life-threatening outcomes.[3] Identifying and treating Meckel's diverticulitis poses significant challenges in rural areas, where diagnostic resources are limited. This report aims to highlight the diagnostic difficulties and emphasize the importance of timely surgical management for Meckel's diverticulitis-induced obstruction. The rarity of symptomatic cases, especially those involving acute obstruction, underscores the clinical significance of this report.[2] This case report highlights the importance of early recognition and surgical management of complicated Meckel's diverticulitis to improve outcomes, particularly in resource-limited environments.

CASE PRESENTATION

A 13-year-old boy presented to the Emergency Department (ED) with complaints of abdominal pain involving the entire abdomen, which had persisted for the past four days. The patient also reported experiencing nausea and vomiting every time he attempted

to eat or drink. Additionally, the boy described a sensation of bloating, and upon physical examination, his abdomen appeared distended and palpably firm. The abdominal X-ray revealed the presence of dilated bowel loops and air-fluid levels on the upright view, indicating the presence of intestinal obstruction (Figure 1). The surgical procedure began with the administration of general anesthesia, and the patient was placed in the supine position. An exploratory laparotomy was performed, revealing a diffuse cloudy fluid throughout the abdominal cavity, indicating contamination. The small intestine appeared to be inflamed. A thorough inspection of the small intestine was conducted, starting from the proximal section at the duodenojejunal junction to the distal ileum (Figure 2).

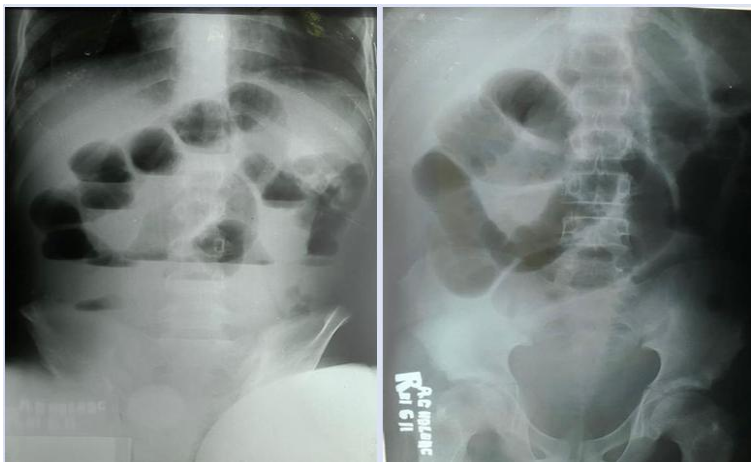

Figure 1. The abdominal X-ray revealed dilated bowel loops and air-fluid levels on the upright view, suggestive of intestinal obstruction, with findings consistent with a diagnosis of Meckel's diverticulosis

First Step: Further exploration, a segment of the distal ileum was found compressed by a mesodiverticular band, affecting approximately 60 cm of the intestinal tract from the proximal to the distal end of the ileum. The obstruction was caused by the entrapment of an intestinal loop within the mesodiverticular band (Figure 2).

Second Step: Releasing the trapped ileal loop by carefully dissecting and freeing the mesodiverticular band from the mesentery. Once the band was removed, the ileal loop was liberated from the diverticulum. The perforated Meckel's diverticulum was subsequently resected to prevent further complications.

Third Step: Intestinal decompression was performed to relieve any remaining obstruction or pressure within the bowel.

Fourth Step: The abdominal incision was closed securely, and the procedure was completed without any immediate complications. The patient will be monitored closely for post-operative recovery, and further management will depend on the histopathological findings and clinical progress.

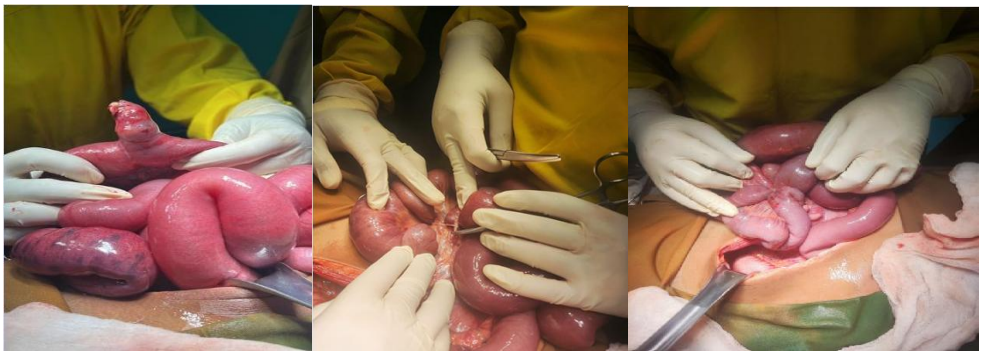

Figure 2. The surgical procedure in a case of Meckel's diverticulum

DISCUSSION

In managing symptomatic Meckel's diverticulum, particularly with obstruction or perforation, the surgical approach plays a pivotal role. In this case, the surgical team performed an exploratory laparotomy, which allowed a thorough examination of the abdominal cavity and identification of both the mesodiverticular band and the perforated diverticulum. This approach contrasts with laparoscopic surgery, which is increasingly favored for uncomplicated Meckel's diverticulum due to its reduced recovery time, smaller incisions, and lower risk of infection. However, in cases involving severe inflammation, perforation, or complex adhesions, open surgery remains the preferred option to ensure better visualization and control.[1,2]

This case report highlights important distinctions in surgical management compared to other documented cases. Skarpas et al. (2020) reported a case where laparoscopic surgery successfully managed small bowel obstruction caused by Meckel's diverticulum. However, laparoscopic techniques are not always applicable, particularly in resource-limited settings like rural hospitals, where diagnostic tools such as CT scans or laparoscopic equipment may not be available. In such scenarios, open surgery remains the gold standard, as seen in this report. Moreover, Huang et al[1]emphasized the role of early diagnosis and minimally invasive procedures in reducing complications.

The present case, however, illustrates the challenges faced in rural settings, where delayed presentation and limited access to advanced imaging can complicate management and necessitate more invasive interventions. The presence of both intestinal obstruction and perforation in this case underscores the importance of prompt surgical exploration, as non-surgical management in similar scenarios could lead to severe outcomes like sepsis or bowel ischemia. The surgical management of complicated Meckel's diverticulum requires precise decision-making tailored to the patient's condition. In this case, an exploratory laparotomy was essential to release the trapped intestinal loop caused by a mesodiverticular band and resect the perforated diverticulum.[4]

Open surgery was chosen due to the presence of perforation and extensive inflammation, a decision supported by recent literature that emphasizes laparotomy for cases involving gangrenous or ulcerated tissue.[5,6]

CONCLUSION

This case demonstrates the importance of individualized surgical strategies for complicated Meckel's diverticulum. Open surgery remains the gold standard for cases

with perforation and severe obstruction, ensuring thorough treatment and reducing the risk of recurrence. Laparoscopic methods, although beneficial for selected cases, are not always appropriate, particularly in emergencies with extensive complications. Early intervention and appropriate surgical planning are critical to improving patient outcomes, especially in resource-limited environments where advanced diagnostic tools may not be available.

DECLARATIONS

All the writers have no conflict of interest in this study publication.

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CASE REPORT

Kikuchi Disease of Parotid Gland

William Stevenson[1*], Nico Lumintang[2], Sherly Tandililing[3]

[1]Department of Surgery, Faculty of Medicine, Universitas Sam Ratulangi, Manado, Indonesia
[2]Department of Head Neck Surgery, Department of Surgery, Faculty of Medicine, Universitas Sam Ratulangi, Manado, Indonesia
[3]Department of Head Neck Surgery, Department of Surgery, Faculty of Medicine, Universitas Sam Ratulangi, Manado, Indonesia

*Corresponding author: doc.stevensons@gmail.com.

ABSTRACT

Aim: Kikuchi disease, often referred to as Kikuchi–Fujimoto disease (KFD), is an uncommon benign cervical lymphadenitis etiology. Cervical lymphadenopathy is Kikuchi disease's most prevalent clinical sign. The incidence of Kikuchi disease is reported more in young adult women. **Case Presentation:** We report a rare instance of parotid gland Kikuchi-Fujimoto disease (KFD). A 36-year-old woman presented to our department with a left preauricular tumor that had been present for three weeks. His Ultrasound revealed a well-defined anechoic cystic lesion with solid components in the preauricular area of the left jugular upper. FNAB was done and the results was an adenoma pleiomorfik with supurative inflammation. The patient underwent parotidectomy surgery and specimens sent to pathologic anatomic department. Patient confirmed with Kikuchi disease of parotid gland based on pathologic examination. **Conclusion:** Although rare, Kikuchi disease can be manifest in parotid gland and mimic parotid gland neoplasm. Complete assessment must be done to make right diagnosis to give appropriate treatment to the patient.

Keywords: Kikuchi disease, parotid gland neoplasm, pathologic examination.

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INTRODUCTION

An uncommon and benign cause of cervical lymphadenitis is Kikuchi disease, commonly referred to as Kikuchi–Fujimoto illness. Most cases have been recorded from East Asia and Japan, with fewer from North America and Europe. According to certain research, the female-to-male ratio for kikuchi sickness can reach 4:1, meaning that it is more common among women. Kikuchi illness usually affects young adults, with a mean age of 20 to 30. The most typical sign of Kikuchi sickness is a very sudden development of cervical adenopathy with fever and a flu-like prodrome.

Kikuchi-Fujimoto disease (KFD) usually lasts one to four months and is self-limited. Kikuchi-Fujimoto illness cannot be definitively diagnosed by laboratory testing. This condition does not show up in a typical way on computed tomography (CT) or ultrasonography exams. Only after a pathologic study can Kikuchi be definitively diagnosed. The purpose of this research is to describe a 36-year-old man who was diagnosed with Kikuchi disease of the parotid gland after developing a lump on his left preauricular region.[1-3]

CASE REPORT

A 36-year-old male patient arrived at our surgical department complaining of a lump on his left preauricular region that had been there for three weeks. Clinical examination results showed a 4x3 cm lump on his left preauricular region that was firm, somewhat movable, and nontender with no indications of inflammation. There was no evidence of

facial nerve paralysis. The systemic examination and the remainder of the head and neck were within normal bounds.

There were no abnormalities in the blood chemistry, erythrocyte sedimentation rate, or complete blood count. A preoperative ultrasound revealed a well-defined anechoic cystic lesions with solid components inside, oval shape, firm borders, size 2.9 x 3.6 cm in the preauricular area of the left jugular upper with non-specific lymph node of left upper jugular.

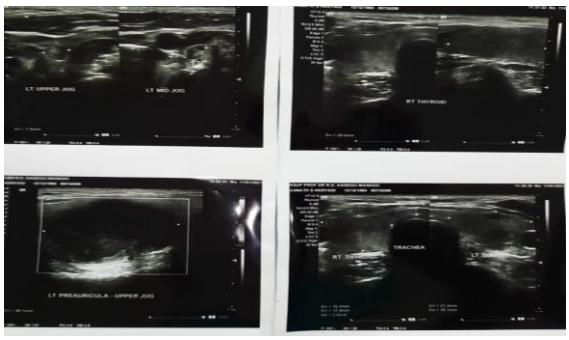

Figure 1. Ultrasound well-defined anechoic cystic lesions with solid components inside

His FNAB result several groups of cells with a spindle nucleus and a round nucleus immersed in the mixoid matrix, the distribution of inflammatory lymphocytes, neutrophils, and necrotic debris. FNAB conclusion was an pleiomorphic adenoma with suppurative inflammation.

The patient underwent surgery under general anesthesia, identification of parotid tumor appeared to firmly bordered at superficial parotid gland. The facial nerve was preserved. The tumor was excised with adequate margin of normal gland tissue. Further identification did not appear to be abnormal. A superficial parotidectomy was performed. Bleeding controlled. Installed redon drain. The surgical wound was closed layer by layer.

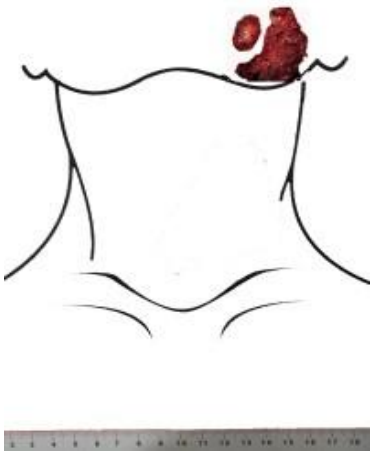

Figure 2. Specimen of parotid tumor and superficial parotid gland sent to pathologic department

On follow up the patient postoperative condition was good with no facial nerve paralysis. Postoperative wound is well, without signs of infection. Would dressing once daily with normal saline moist sterile gauze.

Histopathological analysis of the tumor revealed granulomatous inflammation, foamy histiocytes, karyorrhexis debris (nuclear fraction), and plasma cells with large necrotic areas and eosinophilic mass deposits. No epithelioid cells or Langhans giant cells were found. Pathologic examination final decision was granulomatous inflammation with necrosis tends to be a Kikuchi disease.

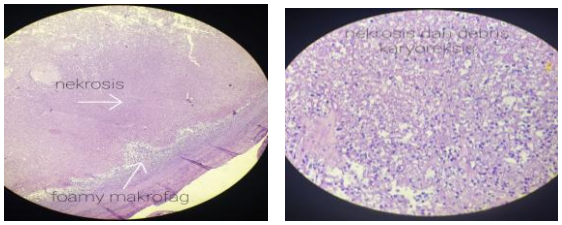

Figure 3. Preparation illustrate foamy histiocytes, necrosis and karyorrhexis debris

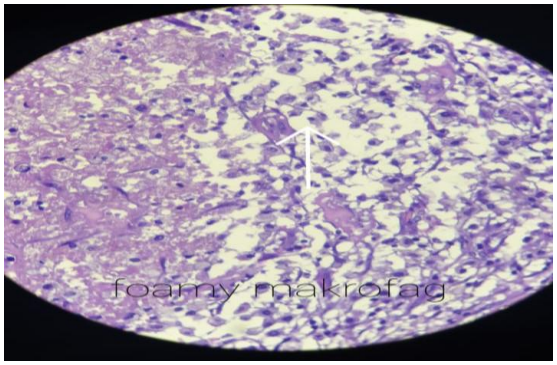

Figure 4. Foamy macrophage.

DISCUSSION

Kikuchi disease, also known as Kikuchi-Fujimoto disease or histiocytic necrotizing lymphadenitis, is a rare, idiopathic, and often self-limiting cause of lymphadenitis. In Japan, Kikuchi initially reported the illness in 1972. In the same year, Fujimoto and associates separately described Kikuchi illness.[1,2]

Kikuchi sickness is rare, however cases have been documented worldwide and in all racial groups. Fewer instances have been recorded from North America and Europe, with the majority coming from East Asia and Japan. According to certain research, the female-to-male ratio for kikuchi sickness can reach 4:1, meaning that it is more common among women. Kikuchi illness usually affects young adults, with a mean age of 20 to 30. The etiology of KFD is a subject of significant conjecture; theories include autoimmune or viral causes.[1,2]

The most common presentation of Kikuchi illness is a very sudden start of cervical adenopathy accompanied by fever and a flu-like prodrome. KFD usually lasts one to four months and is self-limited. There have been reports of a modest recurrence rate of 3% to 4%.[1]

The following are characteristics of lymphadenopathy: [1]

- Although numerous nodal chains may be implicated, 83% of patients have lymphadenopathy that is localized to a single site.
- Eighty percent of patients have impacted cervical nodes, with the posterior triangle cervical nodes accounting for 65–70% of these cases.

Microorganism	Supportive Data	Contrary Data
Yersinia enterocolitica	Positive IIF assay applied to lymphatic tissue in 1 case[24]; positive serologic results reported[23]	Histologic features of mesenteric lymphadenitis differ from those of KFD
Toxoplasma gondii	Positive serologic results reported[25]	Histologic features of toxoplasmic lymphadenitis differ from those of KFD
Epstein-Barr virus	Detected by ISH[19,26] and PCR[19,27]	Not detected by ISH,[27-29] SB,[30] or PCR[31]; 50% positive detection in KFD but also 50% positive detection in control samples by PCR[30]
HHV-6	Detected by PCR[32]	Not detected by PCR[27] or SB[32]; 100% positive detection in KFD but also 50% positive detection in control samples by ISH[32]
HHV-8	23% incidence rate by PCR[33]	Not detected in KFD, but 100% detection in control samples by PCR[33]
HTLV-1	Positive serologic results reported[34,35]	Not detected by ISH or PCR[35]
Hepatitis B virus	None	Not detected by ISH[28]
Parvovirus B19	Detected by immunohistochemical analysis in 1 case[36]	Not detected by immunohistochemical analysis[28]
Herpes simplex, CMV, varicella zoster	None	Not detected by PCR[30,31]

CMV, cytomegalovirus; HHV, human herpesvirus; HTLV-I, human T-lymphotropic virus type I; IIF, indirect immunofluorescence; ISH, in situ hybridization; KFD, Kikuchi-Fujimoto disease; PCR, polymerase chain reaction; SB, Southern blotting.

Figure 5. Microorganisms more frequently reported to have a causative role in KFD.

Extranodal findings:

The thyroid, parotid, myocardium, uvea, and bone marrow are among the infrequently affected extranodal sites. Kikuchi-Fujimoto illness cannot be definitively diagnosed by laboratory testing. This condition does not show up characteristically on computed tomography (CT) or ultrasonography exams.[2]

It is only by histological analysis that Kikuchi-Fujimoto illness may be definitively diagnosed. Typically, Kikuchi Fujimoto illness manifested as a necrotizing condition, with neutrophils either absent or insufficient and patchy or confluent regions of necrosis linked to karyorrhexis. Aspiration with a fine needle cannot definitively diagnose Kikuchi-Fujimoto illness.[1,2]

Histologic finding

Kikuchi disease has three histological stages, which are:[3]

- The proliferative phase includes karyorrhexis, histiocytes, and crescent-shaped nuclei, or crescescentic nuclei.
- Necrotizing phase: widespread necrosis that might disintegrate the lymph node's natural architecture.
- Xanthomatous (foamy cell) phase: the period of recovery when necrosis has been resolved.

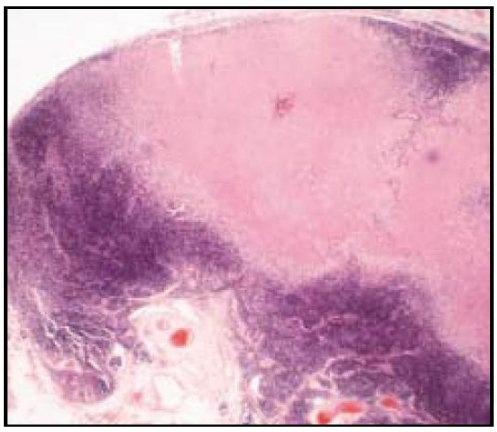

Figure 6. Kikuchi-Fujimoto Disease (KFD) with extensive paracortical area of coagulative necrosis.

Characteristic plasmacytoid monocytes were identified with the use of immunohistochemistry. The latter are natural type 1 interferon-producing cells that are not phagocytic and are most likely engaged in cytotoxic immune responses. Recent research on paraffin-embedded sections utilizing CD68 and HECA-452 antibodies showed that these antibodies, along with CD4, indicated the plasmacytoid monocytes. There has been prior documentation of the co-expression of HECA-452 and CD68 (PG-M1) in plasmacytoid monocytes in Kikuchi's disease.[4]

KFD sufferers do not have a specific therapy. However, as the illness is self-limiting, only symptomatic therapies (such as rest, analgesics, and antipyretics) should be utilized to alleviate distressing local and systemic problems. [5]

In this case report we described a rare presentation of Kikuchi-Fujimoto disease (KFD) in parotid gland. We report a 36 years old man came to our department with swelling on left preauricular area. The onset is subacute evolving during a period of three-weeks. The clinical examination result was a mass measured 4x3 cm without sign of inflammation, firm, moderately mobile and nontender mass on his left preauricular area. No facial nerve paralysis identified.

Ultrasound revealed a well-defined anechoic cystic lesion with solid components inside, oval shape, firm borders, size 2.9 x 3.6 cm in the preauricular area of the left jugular upper with non-specific lymph node of left upper jugular. Patient underwent FNAB examination, the results is an adenoma pleiomorphic with suppurative inflammation. Then he underwent parotid gland tumor removal with superficial parotidectomy. The specimens sent to pathologic anatomic department to confirm diagnosis.

On follow up, pathologic examination results confirmed patient's diagnosis was Kikuchi disease of parotid gland. An enlarged lymph node with paracortical necrotic foci—which are encircled by plasmacytoid monocytes, immunoblasts, and crescentic histiocytes and lack neutrophils—is the pathologic hallmark of Kikuchi's illness. One of the hallmarks of KFD is the presence of nuclear debris, which may be a sign of apoptosis-induced cell death.

CONCLUSION

This case report presented of the 36-year-old man with initial presentation mass on left preauricular for 3 weeks with ultrasound and FNAB of mass suggested parotid gland neoplasm. Pathologic examination of mass revealed Kikuchi disease intra parotid. Diagnosis of Kikuchi disease intra parotid gland was challenging because its presentation mimics parotid gland neoplasm. The definitive diagnosis of Kikuchi only can be made on

pathologic examination. Thus, complete assessment must be done to make right diagnosis to give appropriate treatment to the patient. Awareness of this disorder is important for clinician to prevent misdiagnosis and inappropriate treatment

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DISCLOSURE

The authors affirm no conflict of interest

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CASE REPORT

Simultaneous Extended Right Hemicolectomy and Anterior Resection For Synchronous Colon Cancer: A Case Report

Reinaldo Cendana[1], Gede Eka Rusdi Antara[2]*

[1]General Surgery Resident, Faculty of Medicine, Udayana University/Prof. I.G.N.G Ngoerah General Hospital, Bali, Indonesia
[2]Digestive Division, Department of Surgery, Faculty of Medicine, Udayana University/Prof. I.G.N.G Ngoerah General Hospital, Bali, Indonesia

*Corresponding author: dr_rusdi@yahoo.com.

ABSTRACT

Aim: The aim of this case report was to study the importance of comprehensive examinations of synchronous cancer to avoid repeated surgeries and improved the outcome. **Case Presentation:** a 77-years-old man with sigmoid adenocarcinoma and ascending colon mass was suspected to be a synchronous tumor. The patient complained difficulty in defecation accompanied with weight loss and change of bowel habit, especially hardened and bloody stool. Abdominal CT-scan showed thickened irregular diffuse along the ascending colon to caecum and colonoscopy found circular mass, 30-35cm from the anal verge. The extended right hemicolectomy and anterior resection were performed. There were no notable issues, hence we performed ileal colon and colorectal anastomoses. Pathological result for both specimens were adenocarcinoma. Patient was uneventful and discharged 4 days after the surgery. **Conclusion**: Synchronous CRC was an independent prognostic factor associated with poor overal survival and disease free survival. The primary treatment of synchronous colorectal cancer is surgical resection. Simultaneous right colectomy and anterior resection can be considered for synchronous colorectal malignancies to avoid repeated surgeries, ensuring a similar or potentially improved outcome.

Keyword: synchronous tumor, colon cancer, adenocarcinoma.

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INTRODUCTION

Colorectal cancer ranks as the third most prevalent cancer globally, making up about 10% of all cancer cases. Meanwhile, synchronous colorectal cancers are less frequent and can complicate treatment plans.[1,2] Synchronous colorectal cancer is diagnosed when two or more primary colorectal lesions are identified either simultaneously or within six months of the initial diagnosis. Synchronous colorectal cancer commonly occurs in the sigmoid colon and rectum. More often, it tends to involve the proximal colon, particularly the ascending colon compared to solitary colorectal carcinomas.[3] In this case, Appropriate surgical resection with follow-up colonoscopy examination is recommended. But, colonoscopy alone may impossible to detect synchronous colorectal carcinoma due to the stenosing colorectal carcinoma, small size, or proximity to the main cancer. Therefore, a CT-scan examination is necessary to detect the presence of synchronous cancer.[4] Prompt diagnosis of synchronous colorectal lesions can provide better insight into the treatment plan and potentially prevent repeated surgical resections after the initial treatment.[2]

CASE PRESENTATION

A 77-year-old male came with a chief complaint of difficulty in deffecation accompanied with weight loss and change of bowel habit, especially hardened consistency, pebble-shaped and presence of blood in stool. Prior to the complaint, patient also had

diarrhea with a presence of blood in the stool. Patient had no difficulty to pass a gas. There was no problem with urination and his appetite was still normal. However, patient also admitted to having sudden weight loss, around 8 kgs in the past 3 months.

From initial physical examination, the patient was normotensive, normothermic and had normal heart rate. From the abdominal examination, there was no palpable mass, normal bowel sound, and tympanic percussion finding on all regions of the abdomen. No abnormal finding in rectal toucher. Laboratory results showed mild anemia.

The colonoscopy found a circular mass, around 30-35cm from the anal canal. Then, we performed biopsy with result a low grade adenocarcinoma of the sigmoid (Figure 1). Abdominal CT-scan screening revealed a thickened irregular diffuse along the ascending colon to caecum (Figure 2).

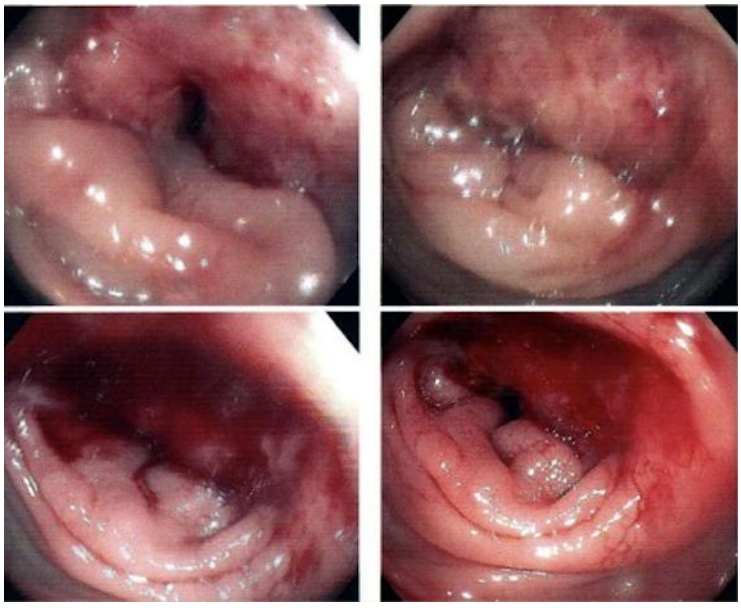

Figure 1. Colonoscopy showed a circular mass in the sigmoid colon, 30-35 cm from the anal verge

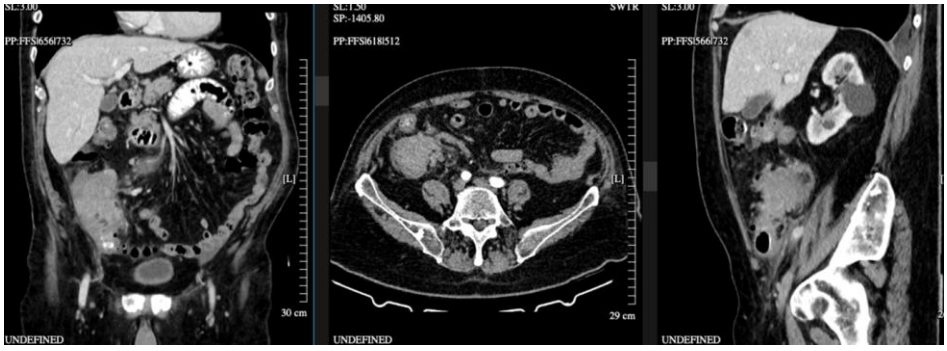

Figure 2. CT Scan showed an irregular diffuse thickening in the ascending colon up to the cecum.

After the series of screenings, we decided to perform a surgery. During the procedure, we found tumor in the ascending colon which infiltrated the sigmoid and ileum. Therefore, we decided to do right extended hemicolectomy, continued with anastomose of the ileum to transverse colon (Figure 3). Upon further evaluation of intra-abdominal cavity, a

tumor was identified on the sigmoid colon. This finding prompted the decision to proceed with a low anterior resection, followed by a rectosigmoid anastomosis. We placed two drains within the subhepatic space and pelvic cavity. Anatomical pathology examination was conducted to assess the resected tissue.

Postoperatively, the patient exhibited no significant complications and was transferred to recovery unit in stable condition. Laboratory tests conducted after the procedure were within normal limits, with no indications of infection or sepsis. On first day after procedure, the patients gad mild abdominal pain consistent with expected postoperative recovery. The patient was discharged on day 4th after surgery in stable condition. Histopathological examination subsequently revealed an adenocarcinoma of the ascending colon. Based on these findings, the case was concluded to represent a synchronous tumor.

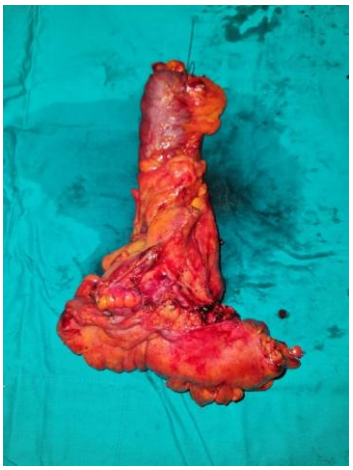

Figure 3. Specimen of right hemicolectomy

DISCUSSION

Colorectal cancer is the third most common malignancy worldwide, accounting for approximately 10% of all cancer cases. However, syncgronous colorectal carcinoma occurs in only about 3.5% of cases.[3] Synchronous colorectal cancer is defined as the presence of two or more primary colorectal tumors diagnosed either simultaneously or within six months of the initial diagnosis. This condition may complicate treatment planning and increase the likelihood of requiring additional surgical interventions.[1,2]

The diagnosis of synchronous malignancies is crucial for optimal treatment planning and may prevent the need for reoperation due to advanced metachronous cancers. In our case, the patient had difficulty in defecation accompanied with weight loss and change of bowel habit which suggest a problem in lower part of abdomen. Significant weight loss also an essential sign of malignancy process. Based on this clinical suspicion, we performed colonoscopy and found a circular mass, around 30-35cm from the anal canal. Then, we continued the screening with abdominal CT-scan and found a thickened irregular diffuse along the ascending colon to caecum. The examination we conducted is consistent with the recommended supplementary diagnostic tests. In this case, we successfully diagnosed the presence of synchronous colorectal carcinoma in the patient, enabling the formulation of an appropriate treatment plan.

The optimal surgical management of patients with synchronous colorectal cancer (CRC) is still debated. Some experts advocate for total or subtotal colectomy, while others recommend targeted surgical resection complemented by regular colonoscopic surveillance. Another option is intraoperative colonoscopy, which allows accurate localization of early mucosal tumors and detection of additional lesions in the proximal colon that may not have been examined, particularly in cases of left-sided obstruction.[5] This approach offers real-time, detailed visualization of lesions during surgery, enhancing the evaluation of disease extent. When one of the synchronous tumors is at an early stage, colonoscopic removal—such as endoscopic mucosal or submucosal

dissection—can be sufficient. Conversely, if the cancers are advanced and widely separated, resection of both colonic segments may be necessary. In our case, because the tumors were far apart, we performed an extended right hemicolectomy with ileotransverse anastomosis, along with a low anterior resection followed by rectosigmoid anastomosis.[4]

Long-term clinical monitoring is often advised for synchronous CRC, depending on available facilities. In this case, the patient recovered well after surgery, returned for follow-up in good condition, and subsequently continued treatment with chemotherapy.

CONCLUSION

A more thorough evaluation and examination are required to establish a diagnosis of synchronous colorectal cancer. Therefore, using both CT-scan and colonoscopy are essential for the early detection of colorectal cancer. Prompt diagnosis of synchronous colorectal lesions can provide doctors with better insight into the patient's treatment plan and potentially prevent repeat surgical resections after the initial treatment.

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DISCLOSURE

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CASE REPORT

JBN Jurnal Bedah Nasional

Thyroid Malignancy in Clinically Benign Cystic Thyroid Nodule Presentation

William Stevenson[1*], Nico Lumintang[2], Sherly Tandililing[2]

[1]Department of Surgey, Faculty of Medicine, Universitas Sam Ratulangi, Manado, Indonesia
[2]Department of Head Neck Surgery, Department of Surgery, Faculty of Medicine, Universitas Sam Ratulangi, Manado, Indonesia

*Corresponding author: doc.stevensons@gmail.com.

ABSTRACT

Aim: Cystic thyroid nodule (CTN) is almost always considered benign (noncancerous). Approximately 1% of people with cystic nodules will develop cancer, but less than 3% of those with partly cystic nodules who do not exhibit any suspicious symptoms will do so. In contemporary clinical practice, the most dependable diagnostic method for choosing patients for surgery is fine-needle aspiration biopsy (FNAC). However, because to the high frequency of insufficient smears and false-negative findings, FNAC has significant limits in instances with CTN. Two patients with cystic thyroid nodules were presented in this case report; however, further anatomical pathology reports following total thyroidectomy surgery revealed that the nodules were malignant. **Case Presentation:** This case report describes two cases of thyroid nodule patients who presented to Prof. Dr. RD Kandou Hospital. These patients had cystic thyroid nodules and subsequently underwent thyroidectomy due to large masses. Pathological examination was conducted and confirmed thyroid malignancy in both cases, specifically follicular variant papillary thyroid carcinoma. **Conclusion:** Ultrasound and FNAC examinations have limitations in detecting thyroid malignancies especially for large cystic thyroid nodule. Large nodule sizes and the inability to sample the whole lesion may potentially contribute to false negative results in FNAC. The experience of the operator also will determine the occurrence of false negatives in the ultrasound. Therefore, as clinician we should be aware there were potency of malignancy even in cystic thyroid nodule cases.

Keywords: cystic thyroid nodules, thyroid malignancy, FNAC, ultrasonography.

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INTRODUCTION

Thyroid nodules are a prevalent endocrine issue observed globally. Thyroid cancer among people under 40 years old was expected to have caused 239,362 cases and 2409 deaths worldwide in 2022. The most prevalent endocrine system cancer and the sixth most frequent cancer globally in women between the ages of 20 and 84 is thyroid cancer.[1]

Thyroid cysts are enlarged areas of the thyroid that are filled with fluid. They can be minor (less than 1 cm) or large and they can occasionally appear very unexpectedly. It is possible for thyroid nodules to be completely cystic, in which case the fluid contains no solid substances. On the other hand, the nodule could be complicated, including both solid and liquid components.[2]

Cystic thyroid nodule (CTN) is almost always considered benign (noncancerous). Approximately 1% of people with cystic nodules will develop cancer, but less than 3% of those with partly cystic nodules who do not exhibit any suspicious symptoms will do so. In contemporary clinical practice, fine-needle aspiration biopsy (FNAC) is the most dependable diagnostic technique for choosing patients for surgery. The high frequency of insufficient smears and false-negative findings, however, means that FNAC has significant limits in patients of CTN.[2] This

study aims to present two patients with cystic thyroid nodules.

CASE REPORT

Case 1. LM/female/56 years old

The patient initially admitted to the hospital because of enlarging lump on anterior neck for 8 years. The lump is slowly growing, not accompanied by pain, no fever, no hoarseness, no shortness of breath, no swallowing difficulties. She did not lose weight in spite of her increased hunger, erratic or fast heartbeat, anxiety, irritability, sleep difficulties, exhaustion, shaky hands, muscular weakness, sweating, difficulty with heat tolerance, or frequent bowel movements. There is no history of severe neck radiation exposure. absence of thyroidal disease in the family.

During the physical examination, blood pressure was within normal limits, pulse was not tachycardic, no tachypnea, there was a mass in the neck at anterior cervical triangle measuring 9x8x6 cm, well-defined borders, cystic consistency, and movement with swallowing. Thyroid function test within the normal range.

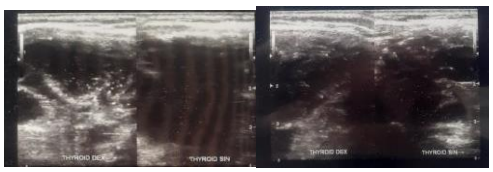

Figure 1. Ultrasound of thyroid showed right and left enlargment, wider – than – tall, visibly border of anechoic masses 9x8x6 cm, regular margin, TIRADS 1.

There were no indications of cancer in the fine needle aspiration biopsy investigation, which revealed cyst cell cells, macrophages, lymphocytes, erythrocytes, and colloidal aggregates.

Total thyroidectomy was performed due to the large size of the tumor and the specimens were sent for histopathological examinations.

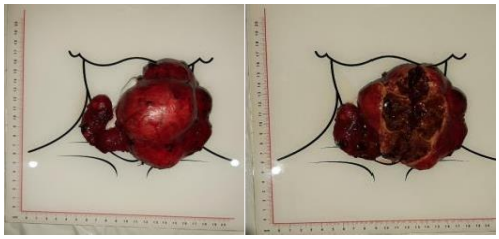

Figure 2. Thyroid tissue 2 nodules size 9x8x6 cm, brown color

The histopathological examination found some cystic dilated follicles, at other focus visible follicles coated by cells with a ground glass core. The conclusion is carcinoma papillary thyroid variant follicular.

Post-surgery, patient complained no hoarseness, no difficulty swallowing, no cramps, or numbness. The patient was discharged on third day. In the next follow-up, the patient was seen at the head and neck surgery outpatient clinic, and the patient's condition was good without postoperative complications.

Case 2. AA/female/56 years old

The patient admitted to the hospital because enlarging lump on the anterior neck for 2 years. The lump is slowly growing, not accompanied by pain, no fever, no hoarseness, no shortness of breath, no swallowing difficulties. Despite having a heightened hunger, an erratic or fast heartbeat, anxiety, irritability, problems sleeping, exhaustion, shaking hands, muscular weakness, sweating, difficulty with heat tolerance, and frequent bowel movements, she did not lose weight. no history of serious neck radiation exposure. no thyroid problems in the family.

During the physical examination, blood pressure was within normal limits, pulse was not tachycardic, no tachypnea, there was a mass in the neck at anterior cervical triangle measuring 8.6 x 6.9 x 8.9 cm, well-defined borders, cystic consistency, and movement with swallowing. Thyroid function test within the normal range.

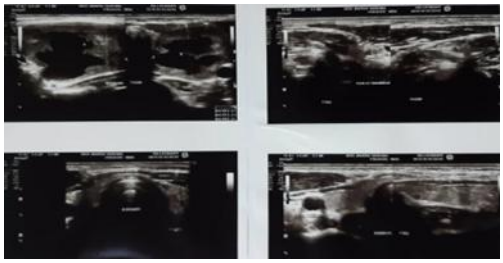

Figure 3. Ultrasound of thyroid showed isoechoic lesions with hypoechoic component, firm boundaries, regular margins without calcification measuring 8.6 x 6.9 x 8.9 cm. On doppler examination does not appear intralesional vascularization (TIRADS III).

An MSCT Scan examination has been carried out with and without contrast with the following results: visible on the right thyroid lobe lesions of iso-dense, heterogeneous with mixed cystic and solid lesions inside, firmly bounded, regular edges. On the post contrast scan, it appears that the enhanced inhomogeneous in the solid component pushing the trachea to the left, the lesion size is 8.6 x 6.9 x 8.9 cm. There were also lesions on the left thyroid with the same characteristics as the mass in the right lobe, measuring 2.3 x 2.6 x 3.3 cm and 2.8 x 3.3 x 3.3 cm. no visible lymph node enlargement. Theconclusion is multiple bilateral thyroid lesions DD/ follicular thyroid adenoma.

One or two clusters of follicular epithelial cells were seen in the fine needle aspiration biopsy test findings, relatively homogeneous, few inflammatory cells and macrophage cysts. The conclusion is Benign Follicular Lesion (Bethesda Category II).

Total thyroidectomy was performed due to the large size of the tumor and the specimens were sent for histopathological examination. The histopathological examination of the tissue was papillary thyroid carcinoma variant folicular.

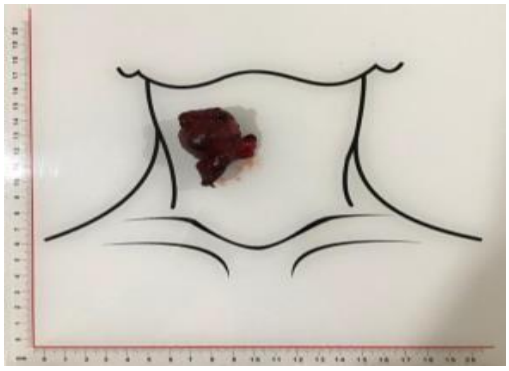

Figure 4. Specimen of nodule thyroid

Post-surgery, patient complained no hoarseness, no difficulty swallowing, no cramps, or numbness. The patient was discharged on third day. In the next follow-up, the patient was seen at the head and neck surgery outpatient clinic, and the patient's condition was good without postoperative complications.

DISCUSSION

Solid nodules that have undergone cystic degeneration make up the majority of thyroid cysts that are clinically palpable; genuine thyroid cysts with a liquid core bordered by cells are uncommon. Usually, these cysts are benign thyroid adenomas. Additionally, it was mentioned that cystic lesions had the same chance of being malignant as solid lesions, and that neither the clinical features of the cysts nor the patient's demographic information can reliably predict this difference. It is advised that the majority of cysts that cannot be removed by aspiration be removed. A fully cystic nodule is thought to be less than 1% malignant, but a partly cystic nodule with no worrisome characteristics is thought to be less than 3%. Yet, since thyroid tumors can sometimes manifest as cystic nodules, their malignant potential should not be disregarded.[2]

Thyroid nodules can be classified as benign or cancerous based on certain ultrasonography

features. A biopsy might not even be necessary if a purely cystic nodule is discovered because its likelihood of being malignant is less than 1%.[2]

If the operator has experience with thyroid ultrasonography, high-definition ultrasonography can yield important information regarding the nodule's features and the risk of cancer.[3]

Because a nodule less than 1 cm is just as likely to have neoplastic cells in the presence of suspicious US findings as a bigger nodule, neither the number of nodules nor their size can be used to predict malignancy.[4]

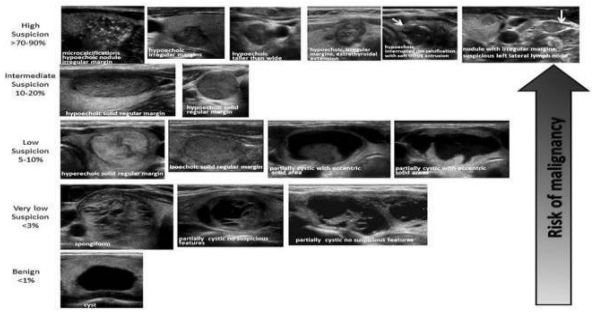

Figure 5. ATA nodule sonographic patterns and risk of malignancy.[5]

The diagnostic FNA results are categorized as follows, according the revised Bethesda System for Reporting Thyroid Cytopathology: follicular or Hurthle cell neoplasm, follicular lesions of uncertain significance or atypia, benign (70%), malignant (5%), and suspected for malignancy. Among the most prevalent benign lesions are lymphocytic thyroiditis, macrofollicular adenoma, and colloid nodules. Papillary thyroid cancer is by far the most common malignant lesion, with high-grade metastatic neoplasms, anaplastic carcinoma, follicular thyroid cancer (FTC), and MTC following.[4, 5, 6]

According to the ATA Recommendation, additional diagnostic testing or therapy is not necessary if the nodule is benign on cytology (strong recommendation, high-quality evidence). However, we must also keep in mind that a number of elements, including as the operator's expertise, the FNA method, specimen preparation, and cytology interpretation, all play a role in an accurate FNAC diagnosis.[6]

The most crucial stage in treating thyroid nodules is fine needle aspiration cytology (FNAC). The sensitivity and specificity of FNAC range from 65% to 98% and 72% to 100%, respectively. False negative rates for cancer range from 1% to 11%, whereas false positive rates range from 0% to 7%. In the event that the lesion is perceptible, FNAC can be carried out free-hand or with ultrasound guidance to boost confidence. The use of ultrasound-guided FNAC is growing in popularity and has been shown to increase FNAC accuracy. With ultrasound-guided FNAC, the acellular or non-diagnostic aspirate is lowered from 14% in free-hand FNAC to 8%. Under ultrasound guidance, FNAC's sensitivity increased from 92% to 98% and its specificity increased from 69% to 71%. Furthermore, lesions smaller than 1 cm, impalpable lesions, or situations where the first free-hand FNAC was non-diagnostic can all be located with the use of ultrasound-guided FNAC.[7]

Clinical monitoring alone can be adequate for thyroid cysts that are benign on FNAC and do not return at follow-up. During follow-up, recurrent thyroid cysts should be aspirated again, and a sample should be sent for cytological analysis. A diagnostic lobectomy may be an option for patients with high risk characteristics identified by history and examination.[7]

Our patients' big nodules may potentially contribute to false-negative results because it is impossible to sample the whole lesion, even when guided by ultrasonography. The most significant cause of erroneous negative

findings is known to be large nodules. Although completely cystic tumors are uncommon, partially cystic lesions are not prevalent in the presentation of papillary thyroid cancer. Numerous factors, including large nodule size (>3–4 cm), bloody cystic fluid, male sex, incomplete cyst resolution, recurrence after repeated aspirations, prior neck irradiation, or radiological findings of local invasion, are actually linked to malignancy and are therefore considered indications for surgery. Cystic thyroid nodules can be classified as benign or malignant based on no broad clinical characteristics.[8]

Aspirated cyst fluid might seem thick, hemorrhagic, or brownish, or it can be clear, watery, and yellow. Since a tumor may overrun its blood supply and experience infarction and cavitation, which implies that the fluid is created from follicular destruction, chocolate-colored aspirates and hemorrhagic are typically thought to be more predictive of neoplasm. The study by Rosen and colleagues found that bloody aspirates were more common in malignant lesions (74%), but they were also observed in 50% of colloid nodules and 38% of benign adenomas. There was no correlation between the aspirated fluid's color or volume and the incidence of cancer in the Cusick et al. trial.[9]

FNAC has a worse diagnosis accuracy for cystic changes of thyroid cancer than it does for solid nodules. Specifically, compared to cystic nodules, which have lower sensitivity and specificity rates (88 and 52%, respectively), solid nodules have significantly better sensitivity and specificity, reaching rates of 100 and 55%, respectively. In this case, additional surgical intervention is strongly advised.[10]

The Belantone research discovered that in 10 out of 119 individuals who had thyroidectomies, the final histology revealed a follicular form of papillary thyroid cancer, even though preoperative cytology had not shown any malignancy. The sensitivity of FNAC in diagnosing this kind of papillary carcinoma is reported to be poor (less than 30%). The most dependable diagnostic method for choosing patients for surgery in modern clinical practice is fine-needle aspiration biopsy (FNAC). However, because to the high likelihood of false-negative results and insufficient smears, FNAC has significant limits when it comes to cystic thyroid nodules.

Up to 50% of smears have been found to be nondiagnostic. The paucity of follicular cells in the cyst fluid and the challenge of collecting a sufficient specimen from the solid section of the wall of CTN may be the causes of the high occurrence of unsatisfactory smears in this condition. In as many as 50% of CTN instances, false-negative findings have been seen, particularly when the nodule is big (>3 cm). It has been found that malignancy rates in cytologically benign simple cysts that returned after aspiration are comparable to those in solid and mixed (solid/cystic) nodules. In the case of CTNs, this potential is especially concerning because a false-negative result suggests a missing malignant tumor. Even under UG, the high nodule size may make it impossible to sample the whole lesion, which might lead to a false-negative result. It has been established that the primary cause of false-negative findings is large nodules.[11]

According to a research by Cooperberg et al., 45% of cases were falsely negative for cystic papillary cancer. Instead of a cytologic misinterpretation, the false negative might be the result of a sample error. As a result, they suggested doing an aspiration biopsy and guiding the needle toward the lesion using sonography.[12]

In our cases, two patients with clinically presented as cystic thyroid nodule that was classified as a benign lesion. However, after

surgery and pathological examination, malignancy was confirmed. In the first case, the patient was identified with an ultrasound as TIRADS 1, which based on the literature is benign with a malignancy potential of < 1%, but upon histopathological examination post-thyroidectomy, follicular variant papillary thyroid carcinoma was found.

In the second case, the patient was identified with an ultrasound as TIRADS 3, which based on the literature is mildly suspicious with a malignancy potential of 13.3%. However, post- thyroidectomy histopathological examination revealed follicular variant of papillary thyroid carcinoma

US had an 81.8% sensitivity and a 91% specificity in detecting malignancy, according to a research by Eisuke Koike et al. Another research by Dhanadia et al. in Gujarat, India, found that ultrasonography had an 83.3% sensitivity and a 72.7% specificity in identifying a malignant lesion. In 2016, Tyagi et al. conducted a research in Uttar Pradesh, India, to identify cancer in the United States. The results showed that the sensitivity was 80%, the specificity was 100%, and the PPV was 100%. According to the Gagandeep Singh Sethi research, US has a 92.31% sensitivity, 97.30% specificity, and 92.31% PPV in detecting a malignant lesion.[13]

In a study by Vinay Raj Thattarakkal et al, that evaluate correlation of TIRADS and Clinicopathological. TIRADS 2, TIRADS 3, TIRADS 4, and TIRADS 5 had risks of malignancy of 4.2%, 13.3%, 57.9%, and 100%, respectively. With a 77.8% sensitivity, 89.6% specificity, 66.6% positive predictive value, and 93.8% negative predictive value, TIRADS categorization proved beneficial in predicting malignancy. The experience of the operator will determine the occurrence of false negatives in the ultrasound examination because ultrasound is an operator-dependent examination.[14]

Large nodule sizes (≥ 3.0–4.0 cm) have been linked to a higher risk of cancer, according to some research, which has supported surgical removal of these nodules. However, other studies have supported the idea that surgery shouldn't be done based only on the size of a big nodule because the incidence of malignancy does not significantly rise when comparing large and small nodules. According to a meta-analysis of 10,817 thyroid nodules by Hammad et al., there was a higher probability of malignancy for nodules between 3.0 and 5.9 cm in size than for those that were 3.0 cm or larger (OR 1.26).[15]

CONCLUSION

Ultrasound and FNAC examinations have limitations in detecting thyroid malignancies especially for large cystic thyroid nodule. The size of the nodule and the inability to sample the whole lesion may potentially contribute to FNAC false negative results. The experience of the operator also will determine the occurrence of false negatives in the ultrasound. Therefore as clinician we should be aware there were potency of malignancy even in cystic thyroid nodule cases.

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DISCLOSURE

The authors affirm no conflict of interest

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REVIEW ARTICLE

Studi Analisis dan *Literature Review* Tentang Perbandingan *Glasgow Outcome Scale-Extended (GOS-E)* dan *Disability Rating Scale (DRS)* dalam Penilaian Hasil Cedera Otak Traumatik

Eko Prasetyo[1], Yovanka Manuhutu[1], Antony Yaputra[2*]

[1] Neurosurgery division, Department of Surgery, Faculty of Medicine, Universitas Sam Ratulangi, Prof. Dr. R.D.Kandou Hospital, Manado, Indonesia

[2] General Surgery Resident, Department of Surgery, Faculty of Medicine, Universitas Sam Ratulangi, Prof. Dr. R.D.Kandou Hospital, Manado, Indonesia

*Corresponding author: antony.yaputra@gmail.com.

ABSTRAK

Tujuan: Penilaian hasil klinis pada pasien dengan cedera otak traumatis (COT) merupakan komponen penting dalam menentukan prognosis dan merencanakan intervensi terapeutik yang tepat. Review artikel ini membahas mengenai perbandingan, kelebihan dan kelemahan *Glasgow Outcome Scale-Extended* (GOS-E) dan *Disability Rating Scal*e (DRS) pada pasien Cedera otak traumatik. **Metode**: Artikel ini merupakan suatu studi literatur yang membahas mengenai kelebihan dan kelemahan GOS-E dan DRS serta pemanfaatannya dalam management cedera otak traumatik. Seleksi artikel dilakukan secara *purposive* dari 20 jurnal. **Hasil:** GOS-E memberikan evaluasi yang lebih terperinci mengenai tingkat pemulihan pasien dengan mengkategorikan hasil ke dalam delapan tingkat, mulai dari kematian hingga pemulihan penuh. Di sisi lain, DRS menilai tingkat disabilitas dan pemulihan dengan fokus pada kesadaran, fungsi motorik, dan aktivitas sehari-hari. Ditemukan bahwa meskipun GOS-E menawarkan detail yang lebih dalam mengenai hasil jangka panjang, DRS lebih mudah digunakan dan lebih cepat dalam administrasi. **Simpulan:** GOS-E dan DRS memiliki kekuatan dalam prediksi luaran jangka Panjang, sedangkan DRS memiliki kelebihan dari segi kemudahan dalam evaluasi dan pengaplikasian. Hasil dari tinjauan ini diharapkan dapat memberikan wawasan yang lebih baik bagi praktisi klinis dalam memilih alat penilaian yang paling sesuai

Kata Kunci: Cedera otak traumatis (COT), *Glasgow Outcome Scale-Extended* (GOS-E), *Disability Rating Scal*e (DRS), prognosis.

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ABSTRACT

Aim: The assessment of clinical outcomes in patients with traumatic brain injury (TBI) is an essential component in determining prognosis and planning appropriate therapeutic interventions. This review article discusses the comparison, advantages, and limitations of the Glasgow Outcome Scale-Extended (GOS-E) and the Disability Rating Scale (DRS) in patients with traumatic brain injury.**Method:** This article is a literature review that examines the strengths and weaknesses of GOS-E and DRS, as well as their utilization in the management of traumatic brain injury. Article selection was carried out purposively from 20 journals. **Results:** GOS-E provides a more detailed evaluation of patient recovery by categorizing outcomes into eight levels, ranging from death to full recovery. On the other hand, DRS assesses the degree of disability and recovery with a focus on consciousness, motor function, and daily activities. It was found that although GOS-E offers more in-depth details regarding long-term outcomes, DRS is easier to use and quicker to administer. **Conclusion:** Both GOS-E and DRS have strengths in predicting long-term outcomes, while DRS has the advantage of being simpler to evaluate and apply. The findings of this review are expected to provide better insights for clinical practitioners in selecting the most appropriate assessment tool.

Keywords: Traumatic brain injury (TBI), Glasgow Outcome Scale-Extended (GOS-E), Disability Rating Scale (DRS), prognosis.

PENDAHULUAN

Penilaian hasil klinis pada pasien dengan cedera otak traumatis (COT) sangat penting untuk menentukan prognosis dan merencanakan intervensi terapeutik. Cedera otak traumatis dapat memiliki dampak jangka panjang yang signifikan terhadap fungsi kognitif, fisik, dan emosional pasien. Oleh karena itu, alat penilaian yang akurat dan dapat diandalkan sangat diperlukan untuk mengevaluasi tingkat pemulihan pasien dan merencanakan rehabilitasi yang tepat.

Dua alat penilaian yang umum digunakan dalam konteks ini adalah *Glasgow Outcome Scale-Extended (GOS-E)* dan *Disability Rating Scale (DRS).* GOS-E adalah pengembangan dari *Glasgow Outcome Scale* (GOS) yang lebih awal, yang dirancang untuk memberikan penilaian yang lebih terperinci mengenai hasil jangka panjang pasien setelah mengalami cedera otak traumatik. GOS-E mengkategorikan pasien ke dalam delapan tingkat, mulai dari kematian hingga pemulihan penuh, yang memungkinkan penilaian yang lebih halus terhadap tingkat kemandirian dan fungsi sosial pasien.[1]

Di sisi lain, DRS adalah alat yang lebih sederhana yang mengevaluasi tingkat disabilitas dan pemulihan pasien setelah cedera otak. DRS terdiri dari delapan item yang menilai kesadaran, fungsi motorik, dan aktivitas sehari-hari, dengan skor berkisar dari 0 (tanpa disabilitas) hingga 29 (kematian).[2] Meskipun DRS lebih mudah dan cepat untuk diadministrasikan, ada kekhawatiran bahwa alat ini mungkin kurang sensitif dalam mendeteksi perubahan kecil dalam status fungsional dibandingkan dengan GOS-E.[3]

Perbandingan antara GOS-E dan DRS sangat penting untuk memahami kelebihan dan kekurangan masing-masing alat dalam konteks klinis. Beberapa penelitian menunjukkan bahwa GOS-E lebih baik dalam memprediksi hasil jangka panjang dan kemandirian pasien, sementara DRS lebih efisien dalam penilaian awal.[4-5] Namun, ada juga penelitian yang menunjukkan bahwa kedua alat ini memiliki validitas dan reliabilitas yang dapat diterima dalam pengukuran hasil pasien.[6-7]

Tinjauan pustaka ini bertujuan untuk membandingkan GOS-E dan DRS berdasarkan dua puluh jurnal akademik, menyoroti temuan kunci, metodologi, dan detail relevan dari setiap studi. Dengan memahami perbedaan dan kesamaan antara kedua alat ini, diharapkan dapat memberikan wawasan yang lebih baik bagi praktisi klinis dalam memilih alat penilaian yang paling sesuai untuk pasien COT.

METODE

Artikel berikut merupakan tinjauan literatur dengan mengumpulkan 20 jurnal yang membahas mengenai penerapan penilaian *Glasgow Outcome Scale-Extended* (GOS-E) dan *Disability Rating Scal*e (DRS) pada pasien cedera otak traumatic (COT). Adapaun seleksi artikel dilakukan secara purposive.

HASIL

Glasgow Outcome Scale-Extended (GOS-E)

GOS-E adalah pengembangan dari Glasgow Outcome Scale (GOS) yang dirancang untuk memberikan penilaian yang lebih terperinci mengenai hasil jangka panjang pasien setelah COT. GOS-E mengkategorikan pasien ke dalam delapan tingkat, mulai dari kematian hingga pemulihan penuh, yang mencakup: 1) Kematian; 2) Status Vegetatif; 3) Disabilitas Berat; 4) Disabilitas Sedang; 5) Disabilitas Ringan; 6) Mandiri dengan beberapa keterbatasan; 7) Mandiri; dan 8) Mandiri dengan aktivitas sosial yang baik. Dengan pendekatan ini, GOS-E memungkinkan penilaian yang lebih halus terhadap pemulihan fungsional pasien, yang

sangat penting dalam konteks rehabilitasi dan perencanaan perawatan jangka panjang.[1,3]

Kelebihan dari GOS-E adalah penilaian yang detail**:** GOS-E memberikan evaluasi yang lebih detail dibandingkan dengan GOS asli, memungkinkan perbedaan yang lebih halus dalam hasil fungsional. Relevansi klinis penggunaan GOS-E dimana GOS-E banyak digunakan dalam penelitian klinis dan praktik untuk mengevaluasi hasil jangka panjang pasien.[2,3]

Kelemahan dari GOS-E antara lain; 1)Penilaian dapat dipengaruhi oleh bias penilai, yang dapat menyebabkan variabilitas antar penilai. Karena bersifat subjektif[2]; 2) Skala ini mungkin memerlukan lebih banyak waktu untuk administrasi dibandingkan dengan skala yang lebih singkat. 3)Sensitivitas terhadap perubahan kecil yang terbatas: GOS-E mungkin tidak mendeteksi perbaikan kecil dalam domain fungsional tertentu.[3]

Table 1. *Glasgow Outcome Scale – Escalated Score.*[2]

GOSE	Interpretasi
1	Meninggal
2	Keadaan vegetatif → Tidak ada kesadaran diri maupun lingkungan
3	Disabilitas berat bawah → Membutuhkan bantuan penuh dalam aktivitas sehari-hari (ADL)
4	Disabilitas berat atas → Membutuhkan bantuan sebagian dalam aktivitas sehari-hari (ADL)
5	Disabilitas sedang bawah → Mandiri, tetapi tidak dapat kembali bekerja/sekolah atau melakukan seluruh aktivitas sosial sebelumnya
6	Disabilitas sedang atas → Masih ada disabilitas, tetapi dapat kembali sebagian pada pekerjaan atau aktivitas sebelumnya
7	Pemulihan baik bawah → Ada defisit fisik atau mental ringan yang memengaruhi kehidupan sehari-hari
8	Pemulihan baik atas → Pemulihan penuh atau hanya gejala ringan yang tidak memengaruhi kehidupan sehari-hari

***Disability Rating Scale* (DRS)**

DRS adalah alat yang digunakan untuk mengevaluasi tingkat disabilitas dan pemulihan setelah cedera otak. DRS terdiri dari delapan item yang menilai kesadaran, fungsi motorik, dan aktivitas sehari-hari, dengan skor berkisar dari 0 (tanpa disabilitas) hingga 29 (kematian). Meskipun DRS memberikan gambaran yang komprehensif tentang kondisi pasien, alat ini cenderung kurang sensitif dalam mendeteksi perubahan kecil dalam status fungsional dibandingkan dengan GOS-E.[4]

Tabel 2. Penilaian *Disability Rating Score.*[4]

Aspek	Kategori & Skor
1. Membuka Mata (Eye Opening)	Spontan (0), Terhadap suara (1), Terhadap nyeri (2), Tidak ada (3)
2. Respons Verbal Terbaik (Best Verbal Response)	Orientasi baik (0), Bingung (1), Tidak tepat (2), Tidak dapat dipahami (3), Tidak ada (4)
3. Respons Motorik Terbaik (Best Motor Response)	Mengikuti perintah (0), Lokalisasi (1), Menarik (2), Fleksi (3), Ekstensi (4), Tidak ada (5)
4. Makan (Feeding)	Lengkap (0), Parsial (1), Minimal (2), Tidak ada (3)
5. Toilet (Toileting)	Lengkap (0), Parsial (1), Minimal (2), Tidak ada (3)
6. Kebersihan diri (Grooming)	Lengkap (0), Parsial (1), Minimal (2), Tidak ada (3)
7. Tingkat Fungsi (Level of Functioning)	Mandiri penuh (0), Mandiri di lingkungan khusus (1), Ketergantungan ringan (2), Ketergantungan sedang (3), Ketergantungan berat (4), Ketergantungan total (5)
8. Kemampuan Bekerja (Employability)	Tidak terbatas (0), Pekerjaan tertentu kompetitif (1), Pekerjaan terlindung/tidak kompetitif (2), Tidak dapat bekerja (3)

Disability Rating Scale (DRS) memiliki beberapa kelebihan. Instrumen ini memberikan penilaian yang komprehensif karena mencakup berbagai aspek disabilitas, sehingga mampu menyajikan gambaran holistik mengenai kondisi pasien. Selain itu, DRS relatif sederhana untuk diadministrasikan dan dapat digunakan oleh berbagai tenaga kesehatan. Dari segi efisiensi, waktu yang dibutuhkan untuk administrasi lebih singkat dibandingkan dengan Glasgow Outcome Scale-Extended (GOS-E).[4–5]

Meskipun demikian, DRS juga memiliki keterbatasan. Skala ini dinilai kurang spesifik karena mungkin tidak cukup sensitif dalam mendeteksi perubahan kecil pada status fungsional pasien jika dibandingkan dengan GOS-E.[5] Selain itu, DRS lebih berfokus pada penilaian disabilitas dibandingkan dengan hasil jangka panjang, sehingga penggunaannya menjadi terbatas dalam konteks tertentu.[6]

Tabel 3. Interpretasi *Disability Rating Score.*[4]

Skor	Kategori
0	Tidak ada (None)
1	Ringan (Mild)
2–3	Parsial (Partial)
4–6	Sedang (Moderate)
7–11	Sedang-berat (Moderately severe)
12–16	Berat (Severe)
17–21	Sangat berat (Extremely severe)
22–24	Keadaan vegetatif (Vegetative state)
25–29	Keadaan vegetatif ekstrem (Extreme vegetative state)
30	Meninggal (Death)

Perbandingan GOS-E dan DRS

Kedua skala, yaitu Glasgow Outcome Scale-Extended (GOS-E) dan Disability Rating Scale (DRS), memiliki kesamaan dalam tujuan utamanya, yakni untuk mengevaluasi hasil pasien dengan cedera otak traumatis (COT) serta memandu intervensi rehabilitasi. Keduanya juga telah terbukti memiliki validitas dan reliabilitas yang dapat diterima dalam berbagai pengaturan klinis.

Namun, terdapat sejumlah perbedaan mendasar antara kedua instrumen ini. Dari segi fokus penilaian, GOS-E lebih menekankan pada hasil jangka panjang dan kemandirian pasien, sementara DRS berfokus pada tingkat disabilitas. Dalam hal detail penilaian, GOS-E menawarkan evaluasi yang lebih terperinci, sedangkan DRS lebih sederhana dan cepat untuk diadministrasikan. Selain itu, kedua skala menggunakan sistem skoring dan interpretasi yang berbeda, sehingga perbandingan langsung antara keduanya menjadi sulit.[7]

Terkait sensitivitas dan responsivitas, DRS terbukti lebih responsif terhadap perubahan klinis selama fase rehabilitasi awal, khususnya pada pasien dengan disabilitas fisik dominan. Sebaliknya, GOS-E lebih stabil dalam mengevaluasi outcome pada 6–12 bulan pasca-cedera, serta lebih sensitif dalam mendeteksi perubahan kognitif. DRS memang memiliki delapan tingkat gradasi disabilitas, berbeda dengan GOS asli yang hanya lima tingkat. Akan tetapi, kompleksitas ini justru mengurangi kepraktisan DRS dalam skrining cepat. Sebaliknya, GOS-E dengan delapan tingkat yang mencakup aspek sosial, lebih efisien digunakan dalam studi berskala besar.[8–10]

Dari sisi validitas dan reliabilitas, studi multi-center menunjukkan bahwa DRS memiliki reliabilitas inter-rater yang lebih tinggi dibandingkan GOS-E. Hal ini disebabkan oleh struktur DRS yang lebih terstandardisasi untuk penilaian fase akut. Meski demikian, GOS-E memiliki validitas prediktif yang lebih baik dalam memproyeksikan outcome jangka panjang, terutama terkait partisipasi sosial pasien. Dari perspektif adaptasi lintas budaya, GOS-E lebih mudah diterapkan karena formatnya

yang sederhana, sedangkan DRS menghadapi tantangan adaptasi akibat kompleksitas item yang berhubungan dengan aktivitas spesifik.[9–10]

Aplikasi Klinis dan Rekomendasi

Dalam konteks aplikasi klinis, Disability Rating Scale (DRS) direkomendasikan terutama pada fase rehabilitasi akut serta untuk pemantauan progres harian. Instrumen ini terbukti efektif dalam menilai tingkat ketergantungan fisik pasien dan kebutuhan intervensi segera. Sebagai contoh, DRS dapat digunakan untuk mengevaluasi respons terapi okupasi pada pasien dengan gangguan kesadaran. Sebaliknya, Glasgow Outcome Scale-Extended (GOS-E) lebih ideal untuk evaluasi jangka panjang, mulai dari satu hingga sepuluh tahun pasca-cedera, serta banyak dimanfaatkan dalam penelitian epidemiologi. Skala ini lebih komprehensif dalam menilai reintegrasi sosial dan kualitas hidup. Contoh aplikasinya adalah studi follow-up untuk menilai keberhasilan program rehabilitasi berbasis komunitas. Beberapa penelitian bahkan merekomendasikan penggunaan GOS-E dan DRS secara komplementer, di mana DRS berfungsi mendokumentasikan kemajuan fungsional awal pasien, sementara GOS-E mengevaluasi outcome sosial dalam jangka panjang.[13]

Dari sisi metodologis, analisis terhadap 20 jurnal yang ditelaah mencakup karakteristik sampel, metode pengumpulan data, analisis statistik, serta potensi bias. Faktor-faktor seperti perbedaan populasi pasien, termasuk usia maupun tingkat keparahan cedera, dapat memengaruhi hubungan yang diamati antara skor GOS-E dan DRS.[14–15] Sintesis temuan dari literatur tersebut menunjukkan adanya korelasi antara kedua skala, meskipun GOS-E sering dianggap lebih sensitif dalam mendeteksi perubahan kecil pada hasil jangka panjang. Validitas prediktif keduanya juga bervariasi tergantung pada konteks klinis.[16–18] Beberapa studi mengungkapkan bahwa GOS-E lebih unggul dalam memprediksi hasil jangka panjang, sedangkan DRS lebih efektif untuk penilaian awal fase rehabilitasi.[19–20]

SIMPULAN

Baik GOS-E maupun DRS berperan penting dalam penilaian hasil pasien COT. GOS-E dan DRS memiliki peran berbeda dalam manajemen COT. DRS unggul dalam reliabilitas dan responsivitas fase akut, sementara GOS-E lebih valid untuk menilai keluaran jangka panjang dan kualitas hidup. Pemilihan skala harus disesuaikan dengan fase pemulihan, tujuan klinis, dan karakteristik pasien. Kombinasi keduanya dapat memberikan perspektif yang komprehensif, mendukung pendekatan holistik dalam rehabilitasi neurologis.

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PERNYATAAN

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