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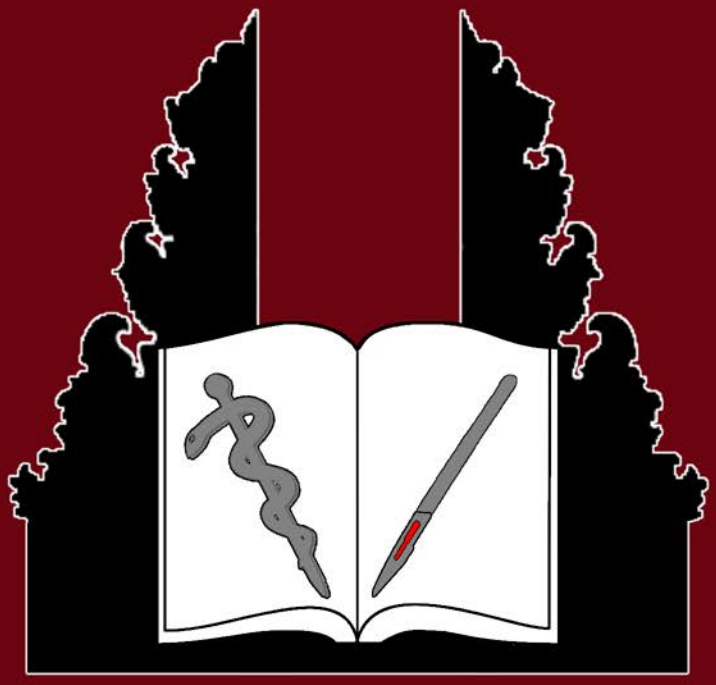

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Pedoman untuk penulis

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*.

Judul agar dibuat dengan HURUF KAPITAL dengan huruf font 14 Times New Roman, sesingkat mungkin, bersifat informatif dan mampu merangkum isi naskah dan tidak berisi singkatan. Di bawah judul disebutkan nama penulis utama dan penulis pembantu, dicantumkan dengan lengkap tanpa gelar, dengan alamat institusi tempat bekerja.

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.

Daftar pustaka dimulai pada halaman baru. Daftar tersebut disusun berurutan, 2 (dua) spasi, menurut kaidah Vancouver dan diberi nomor urut. Daftar pustaka yang dirujuk hendaknya publikasi dalam 10 tahun terakhir, kecuali yang berhubungan dengan data tentang riwayat. Dalam naskah, nomor daftar pustaka ditulis secara superscript. Cara penulisan daftar pustaka merujuk pada *the Uniform requirements for manuscripts submitted to biomedical journals* yang dipublikasi oleh *International Committee of Medical Journal Editors*.

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Volume dengan suplemen
Geraud G, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. *Headache*. 2002;42(Suppl 2):S93-S99.

Bab pada buku
Hahn BH. Systemic lupus erythematosus. Dalam: Isselsbacher KJ, Braunwald E, Wilson JB, dkk, penyunting. *Principles of Internal Medicine*. Edisi ke-14. New York: Mc Graw-Hill; 1998.h.1874-1880.

Boediman I, Wirjodiarjo M. Anatomi dan fisiologi sistem respiratori. Dalam: Rahajoe NN, Supriyatno B, Setyanto DB, penyunting. *Buku Ajar Respirologi Anak*. Edisi ke-1. Jakarta: BP IDAI; 2008.h.1-50.

Buku atau monograf
Korones SB, Bada-Ellzey HS. *Neonatal decision making*. St Louis: BC Decker; 1993.

Seminar atau konferensi
Harnden P, Joffe JK, Jones WG, editors. *Germ cell tumours V*. Proceeding of the 5 th Germ Cell Tumour Conference; 2001 September 13-15; Leeds, UK. New York: Springer; 2002.

Makalah yang sedang dicetak
Sebodo T. Response of plasma and yeast-derived hepatitis vaccines in children. Paediatr Indones. *In press*. 2002.

Tesis / disertasi
Borkowski MM. Infant sleep and feeding: a telephone survey of Hispanic Americans [*disertasi*]. Mount Pleasant: Central Michigan University; 2002.

Internet
Morse SS. *Factors in the emergence of infectious disease*. Emerg Infect Dis [serial online] 1995 Jan-Mar [diakses 5 Juni 1998]. Diunduh dari: http://www.cdc.gov/ncide/EID/eid.htm.

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ORIGINAL ARTICLE

JBN Jurnal Bedah Nasional

Analysis of Disease-Free Survival and Overall Survival of HER2 Positive Subtype Breast Cancer Patients at Prof. Dr. I.G.N.G. Ngoerah Denpasar Hospital

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ABSTRACT

Aim: This study aim to assess the characteristics of the patients, as well as the 3-year and 5-year overall survival and disease free survival of HER2+ breast cancer patients treated at Prof. Dr. I.G.N.G. Ngoerah Hospital Denpasar **Methods:** This retrospective cohort study assessed survival rates and prognostic factors among HER2+ breast cancer patients treated at Prof. Dr. I.G.N.G. Ngoerah Hospital Denpasar from January 2017 to December 2022. The study used medical records to examine variables such as age, tumor characteristics, metastasis patterns, histology, treatments, and survival outcomes over 3- and 5-year periods. **Results:** The 3-year survival rate was 77.7% and the 5-year survival rate was 74.3%, with median survival times of 31 months (95%CI 30.7-32.86) and 49 months (95%CI 47.85-52.089), respectively. Disease-free survival rates indicated median durations of 33 months (95%CI 32.949-34.545) at 3 years and 54 months (95% CI 53.063-56.357) at 5 years. **Conclusion:** This study enhances understanding of HER2+ breast cancer prognosis, emphasizing the critical roles of lymph node status, metastatic burden, and treatment strategies in determining patient outcomes.

Keywords: breast cancer, HER2, survival, prognosis.

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INTRODUCTION

Breast cancer is a global problem, accounting for about a quarter of all cancer cases in women, and is ranked as the fifth leading cause of cancer death. These cancers are categorized into four molecular subtypes: Luminal A, Luminal B, HER2+, and Triple Negative. HER2+ represents approximately 20% of all breast cancer subtypes and is considered the subtype with the worst prognosis until the discovery of HER2 therapies. The incidence of breast cancer is higher in developing countries than in developed countries. Indonesia had a total of 65,858 new cases diagnosed in 2020.[1]

Overall, breast cancer has a good outcome, especially when diagnosed at an early stage. Level of Overall Survival (OS) among patients differs based on molecular subtype and stage.[2–4] Factors affecting OS of HER2+ breast cancer patients include age, tumor size, lymph invasion, number of metastases, type of histology, grade, therapy, ER/PR hormone receptors, and age >75 years. There is an increase in the risk of death in all breast cancer subtypes.[5,6]

The OS at four years among women with HR+/HER2− is estimated at 92.5%, followed by HR+/HER2+ at 90.3%, HR-/HER2+ at 82.7%, and HR−/HER2- at 77.0%. It is well known that HER2 overexpression is

associated with higher disease recurrence and mortality rates. HER2+ breast cancer also has a higher risk of brain metastasis.[7]

The predictors of OS in breast cancer based on previous studies are still debatable. Moreover, there was no OS and disease-free survival (DFS) data for breast cancer patients in Bali. Therefore, we are interested in determining the DFS and OS of HER2 subtype breast cancer patients at Prof. dr. I.G.N.G. Ngoerah Hospital, Denpasar, Bali.

METHOD

A retrospective cohort was conducted to determine 3 and 5-year DFS and OS HER2+ subtype breast cancer patients at Prof. Dr. I.G.N.G. Ngoerah Hospital, Denpasar. All HER2+ subtype breast cancer patients who received treatment from January 2017 to December 2022 were included. Patients with kidney, cardiac, immunological, neurological, or other systemic diseases diagnosed prior to breast cancer diagnosis were excluded from the study. Age, tumor size, lymph invasion, number of metastatic organs, type of histology, TIL, LVI, histopathological degree, and type of therapy data were collected from medical records. Data was analyzed using SPSS version 26. Kaplan-Meier curve analyzed DFS and OS values. All hypothesis tests were carried out in both directions with a significance value of $p<0.05$.

RESULT

There were 300 patients included in this study. The characteristics of the subjects can be seen in **Table 1.** Two hundred and sixty one (87%) were ≥40 years old. The majority of the study subjects had T3 size (70%), N1 (51.7%), and no metastasis (69.7%). Generally, the patients received chemotherapy and surgery (51%). Only 10.3% received chemotherapy, surgery, and anti-HER2. Of the 184 patients who underwent surgery, the majority had grade III histopathology (45.7%), histopathological types other than IDC and ILC (91.3%), LVI negative (69.6%), and TIL positive (71.7%). In the 3-year follow-up, there were 67 patients (22.3%) who died, and 35 patients had relapse (11.7%). At the 5-year follow-up, 77 patients (25.7%) died and 40 patients (13.3%) had relapsed.

Table 1. Characteristics of the Research Subject

Characteristics	Number (%) N=300
Age, n (%)	
<40 years	39 (13.0)
≥40 years	261 (87.0)
Tumor Size, n (%)	
T1	9 (3.0)
T2	81 (27.0)
T3	210 (70.0)
Spread of Lymphnodes, n (%)	
N0	60 (20.0)
N1	155 (51.7)
N2	68 (22.7)
N3	17 (5.7)
Number of Target Organs, n (%)	
None	209 (69.7)
1 Organ	76 (25.3)
≥ 2 Organs	15 (5.0)

Characteristics	Number (%) N=300
Histopathology Type, n=184 (%)	
Invasive ductal carcinoma (IDC)	1 (0.5)
Invasive lobular carcinoma (ILC)	15 (8.2)
Others	168 (91.3)
Degree of Histopathology, n=184 (%)	
Grade I	17 (5.7)
Grade II	83 (45.1)
Grade III	84 (45.7)
Lymphovascular Invasion (LVI), n=184 (%)	
Negative	128 (69.6)
Positive	56 (30.4)
Tumor-Infiltrating Lymphocyte (TIL), n=184(%)	
Negative	52 (28.3)
Positive	132 (71.7)
Treatment, n (%)	
Chemotherapy only	56 (18.7)
Chemotherapy and Anti-HER2	60 (20.0)
Chemotherapy and Surgery	153 (51.0)
Chemotherapy, Anti-HER2, and Surgery	31 (10.3)

The mean DFS in patients with HER2+ subtype breast cancer at 3-year intervals was 33 months (95%CI=32.949-34.545) and at 5-year intervals was 54 months (95%CI=53.063-56.357) (**Table 2**). The mean OS of HER2 subtype breast cancer patients at the 3-year interval was 31 months (95%CI 30.7-32.86) while at the 5-year interval was 49 months (95%CI 47.85-52.089) (**Table 3**). The Kaplan-Meier DFS and OS curves can be seen in **Figure 1** and **Figure 2**, respectively.

Table 2. Disease-Free Survival at 3- and 5-Years

Duration	Disease-free	Relapse	Mean	95% Confidence Interval
3 years	265 (88.3)	35 (11.7)	33.7	32.90-34.54
5 years	260 (86.7)	40 (13.3)	54.7	53.06-56.36

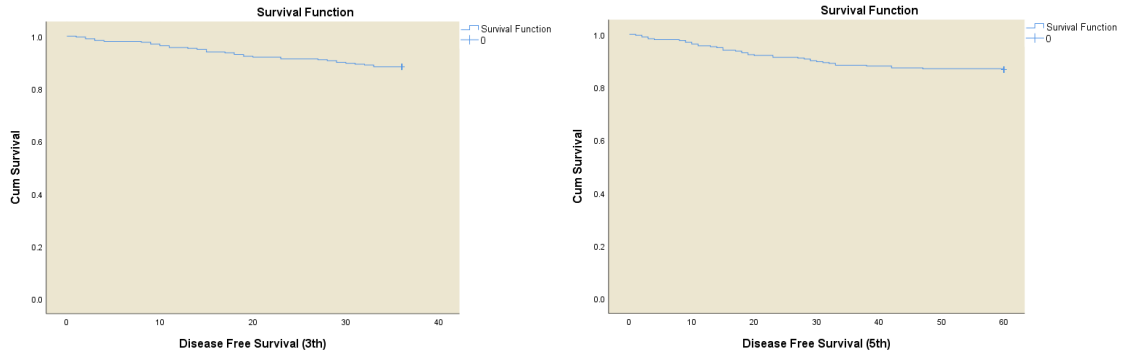

Figure 1. Kaplan-Meier Curve for Disease-Free Survival

Table 3. Overall Survival at 3- and 5-Years

Duration	Live	Die	Mean	95% Confidence Interval
3 years	233 (77.7)	67 (22.3)	31.79	30.7-32.86
5 years	223 (74.3)	77 (25.7)	49.97	47.85-52.09

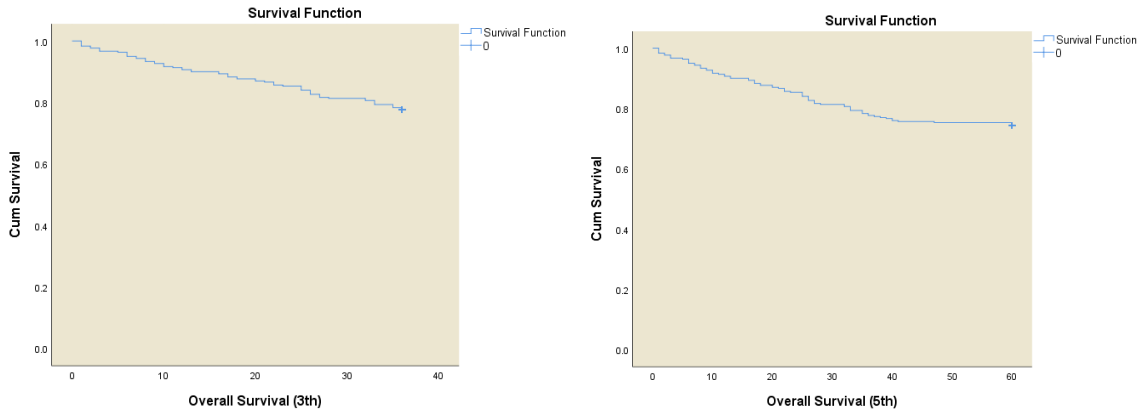

Figure 2. Kaplan-Meier Curve for Overall Survival

DISCUSSION

HER2+ subtype breast cancer patients in this study were dominated by patients ≥ 40 years old (87%). The findings are similar to studies conducted in Ethiopia, Japan, and Norway, where patients over 40 years old dominated more than 50% of the subjects.[3,8,9] The same findings were found in Surveillance, Epidemiology, and End Results (SEER) studies. [5,6]

As many as 70% of the patients in this study had a tumor size of more than 5 cm. In contrast to the findings in other studies where most research subjects had a tumor size of ≤2 cm.[3] Another study conducted in Sweden also showed that the majority of patients in the study had a tumor size of <21 mm.[4]

Studies in HER2+ breast cancer patients showed that the majority of patients had lymph invasion to the unfixed ipsilateral axilla (51.7%) or N1, the remaining 22.7% had spread to the corrected ipsilateral axilla or N2, 5.7% to the ipsilateral infraclavicular or N3, and 20% had no spread or N0. This finding is the same as a study conducted in Japan where The majority of subjects in the study experienced the spread of N1-N3 lymphnodes.[3]

HER2-positive breast cancer patients in this study generally did not metastasize far or to the target organ (69.7%). Only 5% of patients experienced metastasis in ≥ 2 organs, and 25.3% had metastases to 1 target organ. The proportions found in our study are almost identical to those conducted in Ethiopia.[8]

All HER2+ subtype breast cancer patients in this study underwent minimal treatment with chemotherapy. Only 10.3% of the total patients in this study underwent chemotherapy, surgery, and anti-HER2 treatment. The findings in our study are similar to previous studies in which most patients underwent chemotherapy therapy.[10] The patients in the study conducted in Ethiopia also underwent chemotherapy for the most part.[8]

The majority of HER2+ subtype breast cancer patients who underwent surgery, namely 184 patients, had histopathological types other than invasive ductal carcinoma

(IDC) and invasive lobular carcinoma (ILC) (91.3%). In addition, it was found that as many as 84 patients undergoing surgical therapy had grade III, 128 patients had negative Lymphovascular invasion (LVI), and 132 patients were positive for Tumor-infiltrating Lymphocyte (TIL). The findings of IDC and ILC patients were also found by Tesfay et al., where in the study, the majority of patients who underwent surgery had a type of ductal carcinoma in situ. The findings of most patients with grade III were also found in studies conducted in Arabia and Sweden.[4,11] Most patients with LVI negative found in our study were similar to those conducted in France.[12] Research examining the status of TIL shows that patients with TIL > 10% are more common in HER2-positive patients.[13]

This study's survival rate of 3 and 5 years was 77.7% and 74.3%, respectively. The overall survival probability at the three-year and five-year intervals was 0.7767 and 0.7433, respectively. The average overall survival at the interval of three years of this study is 31 months, while the average duration of overall survival at an interval of five years is 49 months. This result is lower than the study conducted in Japan, where it was found 3-year overall survival in the study by 97%.[3] In addition, a study by Elobaid et al. in the United Arab Emirates also has a Survival higher, namely 2-year overall survival breast cancer patients by 97% and 5-year overall survival by 89%.[11] However, the results of our study were higher than those conducted in Ethiopia, where 2-year overall survival and 5-year overall survival were 54.24% and 25.8%, respectively.[8]

Based on cohort data in France, the number of 5-year overall survival HER2+ type breast cancer is higher compared to luminal type and triple-negative breast cancer (TNBC). The findings in the study are associated with the increasing findings of anti-HER2 therapies that are considered to have high effectiveness.[14] Different findings were found in Ukraine and Brazil, where the HER2+ type has Overall Survival smaller than the luminal type.[15,16]

Subtype breast cancer Human Epidermal Receptor Positive (HER2+) was reported to have a lower risk of death compared to the subtype triple-negative breast cancer (TNBC) in a study in Bandung, with a 5-year survival rate of 61.6% and an average overall survival was 34 months.[17] Other research conducted in Makassar also showed that the average Overall Survival HER2+ is higher than TNBC, which is 28 months compared to 27 months.[18] The 5-year survival rate in this study is still higher than the study by the two studies, probably because the study included breast cancer patients of all subtypes. In contrast, this study only included the HER2+ subtype. Therefore, the number of HER2+ subtype breast cancer patients in our study was higher than in the two studies, which affected the percentage of overall survival.

In this study, 3- and 5-year DFS were 88.3% and 86.7%, respectively with the mean DFS for 33 months and 54 months, respectively. The findings in our study follow the study conducted in the UK, where it was found that 4-year disease-free survival in HER2+ subtype breast cancer patients by 89%.[19] The study conducted in Padang found that the proportion of cancer patients who did not experience recurrence was 80% of the total study patients.[20] Average 3-year disease-free survival in our study is also higher than the average in Makassar, which is 22 months.[18]

This study has described the overall survival rate and disease-free survival rate in patients with HER2+ subtype breast cancer at I.G.N.G. Ngoerah Denpasar analyzed for 3 and 5 years. However, this study has some limitations, including the use of anti-HER2 therapy, which is only intended for patients

with metastases of the target organ, and the difficulty of contacting patients to complete data in several patient registers.

CONCLUSION

The values of the 3-year overall survival rate and 5-year overall survival rate in HER2+ subtype breast cancer in this study were 77.7% and 74.3%, respectively, with an average of 31 months (95% CI 30,717-32,863) and 49 months (95% CI 47,852-52,088). This study's average 3-year and 5-year disease-free survival were 33 months (95%CI 32,949-34,545) and 54 months (95%CI 53,063-56,357), respectively. Further research suggests adding other variables that can affect patient survival, such as comorbid diseases suffered and causes of death.

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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.

REFERENCES

1. Globocan. Breast.The Global Cancer Observatory. World Heal Organ. 2020
2. Lyu X, Luo B. Prognostic factors and survival prediction in HER2-positive breast cancer with bone metastases: A retrospective cohort study. *Cancer Med*. 2021;10(22):8114–26.
3. Fujita N, Enomoto Y, Inakami K, Yanagisawa T, Iguchi C, Aono T, *et al*. Prognostic Factors in HER2-Positive Primary Breast Cancer Patients Treated Using Neoadjuvant Chemotherapy Plus Trastuzumab. *Oncol*. 2020; 98(1):35–41.
4. Ellegård S, Engvall K, Asowed M, Hallbeck AL, Elander N, Stål O. Long-term follow-up of early-stage HER2-positive breast cancer patients treated with trastuzumab: A population-based real-world multicenter cohort study. *Front Oncol.* 2022;12:861324.
5. Kim HJ, Kim S, Freedman RA, Partridge AH. The impact of young age at diagnosis (age <40 years) on prognosis varies by breast cancer subtype: A U.S. SEER database analysis. *Breast.* 2022;61:77–83.
6. Cai S, Zuo W, Lu X, Gou Z, Zhou Y, Liu P, *et al*. The Prognostic Impact of Age at Diagnosis Upon Breast Cancer of Different Immunohistochemical Subtypes: A Surveillance, Epidemiology, and End Results (SEER) Population-Based Analysis. *Front Oncol.* 2020;10:1–10.
7. Patel A, Unni N, Peng Y. The changing paradigm for the treatment of HER2-positive breast cancer. *Cancers (Basel)*. 2020;12(8):2081.
8. Tiruneh M, Tesfaw A, Tesfa D. Survival and Predictors of Mortality among Breast Cancer Patients in Northwest Ethiopia: A Retrospective Cohort Study. *Cancer Manag Res.* 2021;13:9225–34.
9. Johansson ALV, Trewin CB, Fredriksson I, Reinertsen KV, Russnes H, Ursin G. In modern times, how important are breast cancer stage, grade and receptor subtype for survival: a population-based cohort study. *Breast Cancer Res*. 2021;23(1):1-10.
10. Weiss A, Menen RS, Lin HY, Shen Y, Rosso KJ, Shaitelman S, *et al*. Factors associated with improved outcomes for metastatic inflammatory breast cancer patients. *Breast Cancer Res Treat.* 2018; 169(3):615–23.
11. Elobaid Y, Aamir M, Grivna M, Suliman A, Attoub S, Mousa H, *et al*. Breast cancer survival and its prognostic factors

in the United Arab Emirates: A retrospective study. *PLoS One*. 2021; 16:1–10.
12. Houvenaeghel G, Cohen M, Classe JM, Reyal F, Mazouni C, Chopin N, *et al*. Lymphovascular invasion has a significant prognostic impact in patients with early breast cancer, results from a large, national, multicenter, retrospective cohort study. *ESMO Open*. 2021;6(6):100316.
13. Sun T, Wang T, Li X, Wang H, Mao Y. Tumor-infiltrating lymphocytes provides recent survival information for early-stage HER2-low-positive breast cancer: a large cohort retrospective study. *Front Oncol*. 2023;13:1–9.
14. Grinda T, Antoine A, Jacot W, Blaye C, Cottu PH, Diéras V, *et al.* Evolution of overall survival and receipt of new therapies by subtype among 20 446 metastatic breast cancer patients in the 2008-2017 ESME cohort. ESMO Open. 2021; 6(3):100114.
15. Movchan OV, Bagmut IY, Shipko AF, Smolanka II, Sheremet MI, Kolisnyk IL, et al. HER2/positive and HER2/low in inflammatory breast cancer recurrence. J *Med Life.* 2022;15(12):1573–8.
16. Marczyk VR, Rosa DD, Maia AL, Goemann IM. Overall Survival for HER2-Positive Breast Cancer Patients in the HER2-Targeted Era: Evidence From a Population-Based Study. C*lin Breast Cancer*. 2022;22(5):418–23.
17. Arnetha TS, Hernowo BS, Adha MJ, Rezano A. Relationship between Molecular Subtypes and Overall Survival of Breast Cancer in Bandung. *Biomed Pharmacol J*.2020;13(3):1543–8.
18. Wijayanto A, Pieter JSLA, Prihantono P, Syamsu SA, Thaufix NS, Abdi A. Survivability Rates Based on Molecular Subtype, Stage and Metastasis of 36 months cohort in Breast Cancer Patients. *Nusant Med Sci J*. 2022;7(1):29–38.
19. Earl HM, Hiller L, Vallier AL, Loi S, McAdam K, Hughes-Davies L, *et al.* 6 versus 12 months of adjuvant trastuzumab for HER2-positive early breast cancer (PERSEPHONE): 4-year disease-free survival results of a randomized phase 3 non-inferiority trial. *Lancet.* 2019; 393(10191):2599–612.
20. Ayuza M, Harahap WA, Rustam R, Nindrea RD. Factors Affecting Disease Free Survival and Overall Survival in Young Breast Cancer Patients in Padang City in 2008 - 2018. *J Andalas' Health*. 2020; 9(1S):65–73.

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ORIGINAL ARTICLE

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The Relationship of Pre- and Post-Operative Kidney Function and The Degree of Hydronephrosis Caused by Stones and Malignancy in Patients who Have Had A DJ Stent Installed

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ABSTRACT

Aim: This study aims to assess the relationships between ureum, creatinine, GFR and the degree of hydronephrosis, both before and after DJ stent installation. This study also assess the association between ureum, creatinine and GFR before and after the DJ stent placement. **Methods:** An analytical observational study with a cross-sectional design was conducted. Patients with hydronephrosis caused by urinary stones in RSUD Ulin Banjarmasin during 1 January 2022 until 31 January 2023 were included. Renal function (ureum, creatinine, GFR) and degree of hydronephrosis data were collected. **Results:** A total of 37 patients were included. Most of them (76,3%) were <60 years old and males (60.5%). There were no significant relationships between ureum, creatinine, and GFR and the degree of hydronephrosis, both before and after DJ stent installation (p> 0.05). There was no significant differences between ureum, creatinine and GFR before and after DJ stent placement. **Conclusion:** There is no significant relationship between kidney function and the degree of hydronephrosis caused by urinary stones.

Keywords: hydronephrosis, ureum, creatinine, GFR, DJ stent.

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INTRODUCTION

The prevalence of nephrolithiasis cases in Asia is around 1–19.1% of the population. The numbers vary based on socio-economic status and geographic location. In Indonesia, the problem of urinary tract stone is still the most common among all urological cases, but there is no national data of the prevalence. Urinary stones that may get stuck in the kidney or urinary tract cause obstruction to the outflow of urine causing an increase in hydrostatic pressure of the collecting system.[1]

Hydronephrosis is a condition that can develop anywhere in the urinary tract, kidney, or meatus urethra. It is caused by anatomical or functional mechanisms that obstruct the flow of urine. Changes in renal blood flow, tubular blood flow, and glomerular filtration

function may result from this rise in ureteral pressure. Most patients with hydronephrosis occur due to small urolithiasis and can be treated by observing and administering acetaminophen. More serious cases with intractable pain may require drainage by placing a Double J nephrostomy or percutaneous stent.[1,2]

Assessment of renal function is important in the treatment of patients with renal disease or pathology affecting renal function. The most used endogenous marker for assessing glomerular function is creatinine. The calculated creatinine clearance is used to provide an indicator of glomerular filtration rate/GFR. The blood urea to creatinine ratio is associated with a decrease in serum creatinine after urinary diversion procedures in obstructive uropathy characterized by hydronephrosis.[1,3]

METHODS

This research was an analytical observational study with cohort retrospective design. The study was conducted following an ethical clearance certificate from Lambung Mangkurat University's Faculty of Medicine and Health Sciences' Health Research Ethics Committee. Thirty-seven patients diagnosed with stones and/or malignancy-induced hydronephrosis in the Surgery Department from January 1, 2022, to January 31 2023 at Ulin Banjarmasin Regional Hospital were included to the study.

The patients used for the study were aged ≥18 years with a diagnosis of hydronephrosis due to urinary tract stones. It was detected using imaging methods (CT-scan and/or USG). Patients had a DJ stent installed and complete examination results data.

Analysis of the relationship between kidney function and degree of hydronephrosis was carried out using the binomial logistic regression test. We used paired t-test in normal distributed data or Wilcoxon test in not normal to analyse the difference of renal function before and after the DJ stent installation. Relative risk and 95% confidence interval 95% were presented. P value less than 0.05 was statistically significant. The statistical analysis was performed using SPSS 26 software.

RESULTS

This study included a total of 37 patients. The majority (76.3%) of patients were <60 years old dan 60.5% were male. The highest degree of hydronephrosis found in patients was grade I (37.8%) (Table 1).

Table 1. Demographic data of research subjects

Variable	n	%
Age		
< 60 years	29	76.3%
> 60 years	9	23.7%
Sex		
Female	15	39.5%
Male	23	60.5%
Degree of hydronephrosis		
I	14	37.8%
II	4	10.8%
III	12	32.4%
IV	7	18.9%

The degree of hydronephrosis before and after DJ stent installation was presented in Table 2. There was a decrease in the proportion of patients with bilateral and unilateral hydronephrosis and an increase in the proportion of patients without hydronephrosis.

Degree of hydronephrosis were regroup to mild (I and II) and severe (III and IV) degree because the number of subjects in each degree was small. Binomial logistic regression test was carried out to analyse the relationship between kidney function and degree of

hydronephrosis before DJ stent installation (Table 3 and 4).

Table 2. Degree of hydronephrosis before and after DJ stent installation

Degree of hydronephrosis	Before DJ stent N(%)	After DJ stent N(%)
Without hydronephrosis	0 (0.0)	10 (27.0)
I	14 (37.8)	4 (10.8)
II	4 (10.8)	14 (37.8)
III	12 (32.4)	7 (18.9)
IV	7 (18.9)	2 (5.4)

Table 3. Ureum, creatinine and GFR levels are based on the degree of hydronephrosis before DJ stent installation

Independent Variable	Mild HN Median (min-max)	Severe HN Median (min-max)
Ureum (mg/dl)	36 (17-56)	39 (24-131)
Creatinine (mg/dl)	1.37 (0.42-3.21)	2.2 (0.5-13.35)
GFR (ml/min1/73 m^2)	47.84 (19.35-125.23)	32.58 (4.92-118.17)

Before DJ stent installation, the creatinine level tends to be higher in patients with severe compared to mild HN degree. On the contrary, the GFR tends to be lower in patients with mild HN degree.

Table 4. Relationship between urea, creatinine and GFR levels with the degree of hydronephrosis before DJ stent installation

Independent Variable	RR	95%CI	p
Ureum (mg/dl)	1.03	0.99-1.07	0.11
Creatinine (mg/dl)	1.77	0.98-3.18	0.06
GFR (ml/min1/73 m^2)	0.98	0.96-1.00	0.07

Before to DJ stent installation, an increase in urea and creatinine levels of 1 mg/dl was associated to an increase in the likelihood of severe HN. A 2% decrease in the incidence of severe HN was associated to a 1 mL/min increase in GFR prior to DJ stent installation. However, these association were not statistically significant (Table 4).

The relationship between kidney function and the degree of hydronephrosis after DJ stent installation was analyzed using a multinomial binomial logistic regression test. These relationships and the results of the analysis are shown in Table 5 and 6.

After DJ stent installation, the levels of ureum and creatinine tend to be higher in patients with severe HN compared to mild HN. In contrast, GFR tends to be lower in patients with severe HN.

Table 5. Ureum, creatinine and GFR levels are based on the degree of hydronephrosis after DJ stent installation

Independent Variable	Without HN Median (min-max)	Mild HN Median (min-max)	Severe HN Median (min-max)
Ureum (mg/dl)	22 (14-29)	23 (14-55)	36.5 (18-98)
Creatinin (mg/dl)	1.14 (0.23-1.23)	1.19 (0.67-3.56)	1.32 (0.65-8.08)
GFR (ml/min1/73 m^2)	69.38 (48.90-228.41)	58.92 (22.46-104.48)	41.36 (8.13-90.90)

Table 6. Relationship between urea, creatinine and GFR levels with the degree of hydronephrosis after DJ stent installation

Independent Variable	RR	95%CI	p
Mild HN vs Without HN			
Ureum (mg/dl)	1.05	0.92-1.20	0.45
Creatinine (mg/dl)	7.04	0.46-107.91	0.16
GFR (ml/min1/73 m^2)	0.97	0.94-1.01	0.11
Severe HN vs Without HN			
Ureum (mg/dl)	1.12	0.98-1.29	0.09
Creatinine (mg/dl)	12.73	0.79-203.86	0.07
GFR (ml/min1/73 m^2)	0.94	0.90-0.99	0.01

After DJ stent installation, an increase in GFR of 1 ml/minute increased risk of mild HN by 3% and a 6% risk reduction of severe HN compared to without hydronephrosis (Table 6). Urea, creatinine and GFR levels did not show significant differences before and after DJ stent installation ($p > 0.05$) based on the Wilcoxon test results (table 7).

Table 7. Comparation of urea, creatinine and GFR levels before and after DJ stent installation

Variable	Before	After	P Value
Urea (mg/dl)	40.84±24.51	42.81±26.69	0.57
Creatinine (mg/dl)	2.55±2.55	2.30±2.56	0.38
GFR (ml/min/1.73 m^2)	48.21±33.04	51.04±28.82	0.32

DISCUSSION

In this study, the majority of patients were <60 years old and male. The highest degree of hydronephrosis found in patients was grade I (37.8%). Hydronephrosis is more common in women aged 20-60 years due to pregnancy and gynecological malignancies. For the age group over 60 years, this disease is more common in men due to prostate disease and its complications.[1,9]

Four categories comprise the Society of Fetal Urology's (SFU) categorization scheme for hydronephrosis; Level 1: only the renal pelvis enlarged. Dilation of the main calyces and renal pelvis is grade 2. Major and minor calyces, as well as the renal pelvis, are enlarged in grade 3. Grade 4: weakening of the renal parenchyma and expansion of the renal pelvis and whole calyx. According to a study at Yemen's Amran Hospital by Alshoabi SA et al., 44.64% of HN was found in the left and 55.36% in the right kidney. Grade 2 HN affected 58% of patients, followed by grade 3 (21.5%), grade 1 (11.6%), and grade 4 (8.2%).[2,9,10]

According to this study, before DJ stent installation, an increase of 1 ml/min GFR was associated with a 2% reduction in the risk of experiencing grade 3 and 4 HN, but this relationship was also not statistically significant. A study by Shehab et al. study split the patient into two groups: group 1 received ureteral stent placement, while group 2 received other forms of care. Prior research has demonstrated the utility of renal GFR as a gauge for improved renal function following ureteral stenting. Compared to 61 kidneys (66.3%), 56 (71.8%) in group 1 had much

better kidneys. The statistically significant association were found in group 2 between renal perfusion and renal recovery as well as between parenchymal thickness and recovery in both groups. The association between degree of corticomedullary differentiation and recovery and hemoglobin levels between presentation and recovery were also found to be statistically significant.[3,8,11]

A study at Cipto Mangunkusumo Hospital in Jakarta reported a statistically significant correlation between the success of DJ stent implantation and the ratio of blood urea to serum creatinine, where there was a decrease in both parameters. In cases of obstructive uropathy with hydronephrosis, the blood urea to creatinine ratio is associated to a decrease in serum creatinine following urinary diversion treatments. Changes in the blood urea and creatinine ratio, which is used to gauge the severity of renal impairment in patients, could be the result of treatment delays in presenting patients. In addition, Renal parenchymal thickness and blood urea were found to have a statistically significant relationship with serum creatinine in good surgical outcomes as evidenced by a decrease in postoperative creatinine.[4,12,13] This study found that the increase of urea and creatinine level and decrease of GFR associated with HN risk, however the results were not statistically significant.

Prior research reported increase GFR following obstruction removal.[5,19,20] Meanwhile, there was no significant association between kidney function and the degree of HN, before and after DJ stent installation in this study. This may because of the difference time when the ultrasound was performed and the kidney function samples were taken. That may also because of the differences in the homogeneity and distribution of data.

Study by Goertz and Lotterman[20] reported a correlation between the size of ureteral stones on CT scan and the degree of HN seen on focused emergency ultrasonography.[14,15] Sasmaz et al.[19] found that a higher percentage of ureteral stones larger than 5 mm was associated to higher degree of HN on ultrasonography.[19] The majority of study participants had mild or non-existent HN; these individuals also typically had larger ureteral stones. When used in the emergency room, ultrasonography had a specificity of 78.5% for detecting no or mild HN and an 87.6% negative predictive value for ureteral calculi ≤5 mm. The requirement for CT would be reduced by 73% if it were not done in all patients without or with mild HN, as stones <5 mm usually pass naturally.[16,17,18]

Not significant result in this study might also due to confounding factors such as diabetes nephropathy as comorbid disease. Diabetic nephropathy, one of diabetes mellitus complication, affects the normal function of the kidneys in removing waste products and extra fluid from the body. Diabetic nephropathy slowly damages the kidney's filtering system. Faster treatment can prevent or slow this condition and lower the chance of complications. Diabetic kidney disease can cause kidney failure. This is also called end-stage renal disease.[6,21,22]

Serum creatinine is currently one of the most significant indicators of renal function. Creatinine can be filtered through the glomerulus because of its small size and rarely absorbed in the renal tubules. The majority of creatinine is eliminated through urine. When a person has renal failure, their body builds up creatinine, which can be harmful. Kidney function is reflected in the estimated glomerular filtration rate, or eGFR. This measure of the glomerulus's filtering capacity in milliliters per minute is used to evaluate the kidneys' capacity to eliminate metabolic waste

from the body. Serum creatinine has certain limitations as an indication, nevertheless. Serum creatinine, in particular, is not a timely or reliable indicator of renal function. Only when a significant portion of the kidney is pathologically damaged and the glomerular filtration rate is decreased by more than 50% does an increase in serum creatinine become clinically apparent. As a result, in the early stages of the disease, serum creatinine does not accurately represent changes in renal function.[8,25]

CONCLUSION

There is no relationship between kidney function and the degree of hydronephrosis caused by stones in hydronephrosis patients who have had DJ stents installed. There is no significant difference between urea levels, creatinine levels, and GFR before and after DJ stent installation in patients with hydronephrosis due to stones.

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DISCLOSURE

There were no known competing financial interests or interpersonal ties that would have seemed to have an impact on this paper's work report.

This article have the ethical clearance from The Health Research Ethics Commission of the Faculty of Medicine at Lambung Mangkurat University in Banjarmasin, Indonesia, has deemed this study to be ethically feasible. (UP–KTI No. 046/KEPK-FK ULM/EC/IV/2024.

REFERENCES

1. Thotakura R, Anjum F. Hydronephrosis and Hydroureter. In: StatPearls. Treasure Island (FL): *StatPearls Publishing*; (online article) 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK563217/
2. Gounden V, Bhatt H, Jialal I. Renal Function Tests. In: StatPearls. Treasure Island (FL): *StatPearls Publishing*; (online article) 2023. Available at: https://www.ncbi.nlm.nih.gov/books/NBK507821/
3. Pérez-Fentes D, Aranda-Pérez J, de la Cruz JE, et al. Indications, Complications and Side Effects of Ureteral Stents. In: Soria, F., Rako, D., de Graaf, P. (eds) Urinary Stents. *Springer*. 2022.
4. Chewcharat A, Curhan G. Trends in the prevalence of kidney stones in the United States from 2007 to 2016. *Urolithiasis*. 2021;49(1):27-39.
5. Nojaba L, Guzman N. Nephrolithiasis.. In: StatPearls [Internet]. Treasure Island (FL): *StatPearls Publishing*; (serial online) 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559227/
6. Cunningham P, Noble H, Al-Modhefer, AK, et al. Kidney stones: Pathophysiology, diagnosis and management. *Br J Nurs*. 2016;25(20): 1112-6.
7. Washington IM, Van HG. Clinical Biochemistry and Hematology. The *Laboratory Rabbit, Guinea Pig, Hamster, and Other Rodents*. 2012;57-116.
8. Keays MA, Guerra LA, Mihill J, et al. Reliability assessment of Society for Fetal Urology ultrasound grading system for hydronephrosis. *J Urol*. 2008;180 (4): 1680-2.
9. Isarangkul D, Wiyakrutta S, Kengkoom K, et al. Mitochondrial and cytoskeletal

alterations are involved in the pathogenesis of hydronephrosis in ICR/Mlac-hydro mice. *Int J Clin Exp Med*. 2015;8(6):9192-204.
10. Shehab M, El Helali A, Abdelkhalek M, et al. Role of ureteric stents in relieving obstruction in patients with obstructive uropathy. *Urol Ann*. 2013;5(3):148-51.
11. Xie T, Zhou H, Gao Y, et al. Serum and Urinary Neutrophil Gelatinase-Associated Lipocalin Levels as Early Markers of Renal Function in Patients with Urinary Stone-Induced Hydronephrosis. *Front Surg*. 2022; 9:843098.
12. Alshoabi SA, Alhamodi DS, Alhammadi MA, et al. Etiology of Hydronephrosis in adults and children: Ultrasonographic Assessment in 233 patients. *Pak J Med Sci*. 202;37(5):1326-30.
13. Assimos D, Crisci A, Culkin D, et al. Preoperative JJ stent placement in ureteric and renal stone treatment: results from the Clinical Research Office of Endourological Society (CROES) ureteroscopy (URS) Global Study. *BJU international*. 2016;117(4):648-54.
14. Yang Y, Tang Y, Bai Y, et al. Preoperative double-J stent placement can improve the stone-free rate for patients undergoing ureteroscopic lithotripsy: a systematic review and meta-analysis. *Urolithiasis*. 2018;46(5):493-9.
15. Basulto-Martínez M, Klein I, Gutiérrez-Aceves J. The role of extracorporeal shock wave lithotripsy in the future of stone management. Curr *Opin Urol*. 2019;29(2):96-102.
16. Moak JH, Lyons MS, Lindsell CJ. Bedside renal ultrasound in the evaluation of suspected ureterolithiasis. *The Am J Emerg Med*. 2012;30(1):218-21.
17. Inci MF, Ozkan F, Bozkurt S, et al. Correlation of volume, position of stone, and hydronephrosis with microhematuria in patients with solitary urolithiasis. *Med Sci Monit*. 2013;19:295-9.
18. Mefford JM, Tungate RM, Amini L, et al. A comparison of urolithiasis in the presence and absence of microscopic hematuria in the emergency department. *West J Emerg Med*. 2017;18(4):775.
19. Sasmaz Mİ, Kirpat V. The relationship between the severity of pain and stone size, hydronephrosis and laboratory parameters in renal colic attack. *The Am J Emerg Med*. 2019;37(11):2107-10.
20. Goertz JK, Lotterman S. Can the degree of hydronephrosis on ultrasound predict kidney stone size?. *The Am J Emerg Med*. 2010;28(7):813-6.
21. Soeroto AA, Situmorang GR and Rasyid N. Predictive factor of renal function recoverability in upper-tract obstructive uropathy after percutaneous nephrostomy and Double -J stent insertion in Indonesian National Referral Hospital *F1000Research.* 2022; 11:1146.
22. Danarto R. Patient Prognosis After Relief of Obstriction. *J Med Sci*. 2018;50(4):392-399.
23. Wu K, Chen Y, Chen M, Chen Y. Clinical factors predicting ureteral stent failure in patients with external ureteral compression. *Open Medicine*. 2021;16(1):1299-1305.
24. Sataa S, Kerim C, Sami B, et al. Giant hydronephrosis in adults: what is the best approach? Retrospective analysis of 24 cases. *Nephrourol Mon*.2011; 3:177–81
25. Wang R, Wu Z, Liu H, et al. Influence of Hydronephrosis on GFR among patients with Renal Injury. *Journal of Nuclear Medicine*. 2018;59(Supplement 1):380.

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ORIGINAL ARTICLE
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The Association Between Preoperative Serum Thyroid-Stimulating Hormone and Neutrophil-Lymphocyte Ratio as Predictors of Papillary Thyroid Cancer

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ABSTRACT

Aim: This study aims to evaluate the correlation between blood thyroid stimulating hormone levels and neutrophil lymphocyte ratio prior to thyroidectomy in patients with papillary thyroid cancer, as well as the potentiality of those as predictors of papillary thyroid cancer. **Methods:** Thyroid nodule patients over the age of 18 who received treatment at Prof. Dr. R.D. Kandou General Hospital between 2020 and 2024 and who fulfilled the requirements for research inclusion underwent thyroidectomy surgery. The study used a retrospective, descriptive-analytical strategy. **Results:** The association between TSHs and papillary thyroid cancer was significant with a p-value of 0.025, sensitivity of 51.1%, and specificity of 73.9%; the ROC analysis was performed for TSHs with the results of the AUC value analysis = 0.634 (95% CI: 0.518 – 0.749) with p value = 0.028; NLR and papillary thyroid cancer was significant with a p-value <0.001, sensitivity of 68.9%, and specificity of 100%; the ROC analysis was performed for NLR values with the results of the AUC analysis value = 0.852 (95% CI: 0.766-0.938) with p value = <0.001. **Conclusion:** NLR is advised as a better predictor of papillary thyroid cancer than TSHs.

Keywords: NLR, TSHs, predictors of papillary thyroid cancer.

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INTRODUCTION

Thyroid cancer is the most common endocrine malignancy. Over the past three decades, the incidence of thyroid cancer has tripled in the United States and developing countries worldwide. Early diagnosis and management are crucial for thyroid cancer.[1]

Inflammation has been linked with the development of many cancers and is involved almost all of the pathogenic steps of malignancy initiation and propagation including its dissemination. An elevated ratio of Neutrophils-to-Lymphocytes (NLR) is the simplest marker of systemic inflammatory response.[2]

We decided to investigate relationship between neutrophil-lymphocyte ratio and preoperative serum thyroid-stimulating hormone as predictors of papillary thyroid cancer because no prior research between these two variables and easily applicable test in clinical practice. Therefore, this study aims to evaluate the correlation between blood thyroid stimulating hormone levels and neutrophil lymphocyte ratio prior to thyroidectomy in patients with papillary thyroid cancer, as well as the potentiality of those as predictors of papillary thyroid cancer

METHODS

This study is a descriptive-analytic study with a retrospective approach. The target population for this study consists of Thyroid nodule patients over the age of 18 who received treatment at Prof. Dr. R.D. Kandou General Hospital between 2020 and 2024. The

age criterion of >18 years is selected due to the high incidence of thyroid nodules in this age group.

The inclusion criteria in this study: 1) Patients over 18 years of age with thyroid nodules who sought treatment at the surgery clinic of Prof. Dr. R.D. Kandou General Hospital, 2) Patients who underwent preoperative TSH and NLR examinations prior to thyroidectomy, 3) Patients who underwent thyroidectomy surgery, and 4) Patients who underwent histopathological examination of thyroid tissue post-thyroidectomy

Meanwhile, the exclusion criteria in this study are: Patients with clinical hypothyroidism, clinical hyperthyroidism, acute infectious diseases, Hashimoto's Thyroiditis, levothyroxine, antithyroid drugs, corticosteroids, or other immunosuppressive medications.

The sample size calculation was based on this equation:

$$n = \left[\frac{Z\alpha + Z\beta}{0.5 \ln \frac{1+r}{1-r}}\right]^2 + 3$$

Explanation:

- n: sample size
- α: Type I error set at 5%, giving Zα=1.96
- β: Type II error set at 20%, giving Zβ=0.84
- r: correlation coefficient between the two variables in the study, set at 0.19
- The value of r = 0.19, r is based on a study by Huang et al., with p<0.0001
- ln: natural logarithm

Based on the sample size formula, the minimum sample size required for this study is 90 participants. The sampling technique used in this study is purposive sampling. Subjects who meet exclusion criteria will not be included as samples.

The independent variables in this study are Preoperative thyroid stimulating hormone (TSH) Levels and Preoperative Neutrophil-to-Lymphocyte Ratio (NLR). Meanwhile, the dependent variable in this study is Papillary Thyroid Cancer.

Preoperative Neutrophil-Lymphocyte Ratio (NLR) is the ratio number between absolute neutrophil count and absolute lymphocyte count measured preoperative thyroidectomy. Preoperative TSH test is TSH hormone levels using a blood sample taken from a vein in the patient's arm preoperative thyroidectomy. Papillary Thyroid Cancer (PTC) is malignant neoplasm of thyroid follicular cells with papillary growth pattern on histopathology examination

The data collection process in this study is as follows: 1) Obtain permission and inform relevant parties, such as Prof. Dr. R.D. Kandou Hospital and the Hospital Ethics Committee, about the purpose and benefits of the research, 2) Select patients with thyroid nodules who are receiving treatment at the Surgery Clinic of Prof. Dr. R.D. Kandou Hospital. Data will be collected from patients who undergo thyroidectomy surgery and have histopathological examination of thyroid tissue, 3) Patients who meet the inclusion criteria will be included in the research sample, 4) Data on preoperative NLR and serum TSH levels will be taken from laboratory examination results, 5) Patients who do not meet the inclusion criteria or who meet exclusion criteria will be excluded from the study, 6) Data recording and analysis will be conducted, 7) Data will be reported.

The data processing will mostly be done using the SPSS statistical software (version 27.1). As an initial step, raw data will be entered into a Microsoft Excel file, which provides a comprehensive and user-friendly

platform for data entry. The subsequent data processing and all statistical analysis will be performed using this statistical software. The data is presented in tabular form and graphic accompanied by a descriptive explanation.

Data collection will take place at Prof. Dr. R.D. Kandou General Hospital in Manado. Information will be obtained from medical records after the researcher has received approval from the Ethics Committee of Prof. Dr. R.D. Kandou Hospital.

RESULTS

Characteristics of research subjects

Based on age distribution (**Table 1**), the average age of the research subjects was 54.58 years with a standard deviation of 12.555. According to gender distribution, the majority of the samples were female, with 58 individuals (63.7%), while 33 individuals (36.3%) were male.

Table 1. Characteristics of Age and Gender of Research Subjects

Characteristics	Minimum	Maximum	Mean	SD
Age	26	80	54.58	12.55
Gender	**Sum**	**Percentage (%)**		
Male	33	36.3		
Female	58	63.7		
Total (n)	91	100		

Based on the results of the histopathological examination (**Table 2**), among the 91 research samples, 45 subjects (49.5%) were confirmed to have papillary thyroid cancer, and 46 subjects (50.5%) had benign thyroid nodules.

Table 2. Neoplasm Type Based on Histopathological Results

Neoplasm type	Frequency (n)	Percentage (%)
Papillary thyroid cancer	45	49.5
Benign thyroid nodule	46	50.5
Total (n)	91	100

Table 3 shows the laboratory results for NLR and TSH levels in the study. The lowest NLR value was 1.11, the highest was 5.07, with an average of 2.4846 and a standard deviation of 1.08190. For the TSH levels, the lowest value was 0.74 mIU/L, the highest was 2.63 mIU/L, with an average of 1.5601 mIU/L and a standard deviation of 0.48493.

Neutrophil/Lymphocyte Ratio and TSH of Research Subjects

Table 3 shows the laboratory results for NLR and TSH levels in the study. The lowest NLR value was 1.11, the highest was 5.07, with an average of 2.4846 and a standard deviation of 1.08190. For the TSH levels, the lowest value was 0.74 mIU/L, the highest was 2.63 mIU/L, with an average of 1.5601 mIU/L and a standard deviation of 0.48493.

The Association Between TSH and Papillary Thyroid Cancer

A chi-square analysis of the association between TSHs and papillary thyroid cancer revealed a significant p-value of 0.025, sensitivity of 51.1%, and specificity of 73.9%.

Table 3. Preoperative NLR and TSHs Examination Results

Examination type	Minimum	Maximum	Mean	SD
Pre-operative NLR	1.11	5.07	2.4846	1.08
Pre-operative TSHs	0.74	2.63	1.5601	0.48

The Association Between Papillary Thyroid Cancer And NLR

NLR and papillary thyroid carcinoma were significantly correlated, according to chi-square analysis, with a p-value <0.001, a sensitivity of 68.9%, and a specificity of 100% (**Figure 1**).

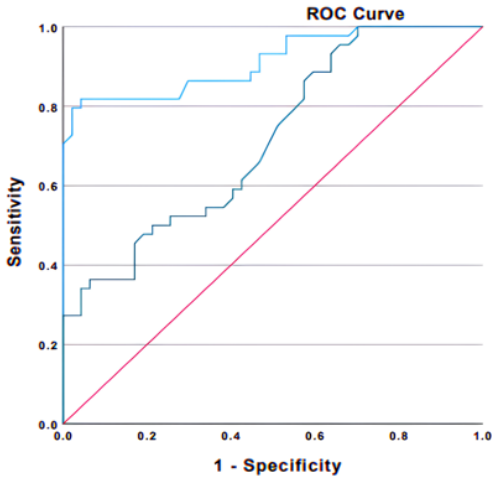

Figure 1. Sensitivity and Specificity for NLR (light blue) and TSH (dark blue).

DISCUSSION

Regarding the distribution of gender, the majority of the respondents were female, with 58 individuals (63.7%), and male respondents numbered 33 (36.3%). This finding is consistent with the literature, which states that malignant thyroid nodules occur three times more often in women than in men. In our study, the average age of the subjects was 54.58 years, with the youngest being 26 years old and the oldest 80 years old. These findings consistent with the study by Maulana et al., where thyroid nodules were found to be more common in women than men, with an average age of 50.54 ± 13.8 years.[3]

Kim studied 1,759 patients with differentiated thyroid carcinoma who underwent thyroid surgery at Chonnam National University Hwasun Hospital. Serum TSH levels were significantly higher in patients with thyroid carcinoma compared to the control group, with average TSH levels of 1.95 ± 0.9 mIU/L and 1.62 ± 0.8 mIU/L, respectively ($p < 0.001$).[4]

Both benign and malignant thyroid tumours express functional TSH receptors on the plasma membrane, and in vitro studies have shown that TSH increases adenylate cyclase activity, leading to cAMP production and cell growth through receptor stimulation. Thyroid stimulating hormone levels were higher in patients with thyroid cancer compared to those with benign nodules. The risk of malignancy in patients with thyroid nodules increased with serum TSH concentrations, even within the normal range. Papillary thyroid carcinoma expresses TSH receptors. TSH, through interaction with TSH

receptors, is a major growth factor for the thyroid.[5–8]

In our study, the serum TSH values ranged from 0.74 to 2.63, with a mean of 1.5601 and a standard deviation of 0.48493. Based on the ROC analysis, the AUC for TSH was 0.634 (95% CI: 0.518–0.749) with a p-value of 0.028. This indicates a significant relationship between serum TSH levels and the risk of papillary thyroid cancer. Our findings are consistent with the studies conducted by Golbert et al., and Hannah Nieto.[5,9]

A study by Golbert et al. examined 615 thyroid nodule patients. Thyroid cancer was found in 47 patients (29.4%) out of 160 who had thyroidectomies. Regardless of the testing method, cancer patients had higher average blood TSH levels than patients with benign nodules: 2.25 vs. 1.50 (CLIA; $p = 0.04$) and 2.33 vs. 1.27 (ECLIA; $p = 0.03$).[5]

Hannah Nieto et al. found that the risk of malignancy increased with elevated serum TSH levels. Nieto found that preoperative serum TSH concentration could independently predict the presence of malignancy in patients with thyroid nodules. TSH measurement to identify high-risk thyroid nodules in routine clinical practice is an interesting, cost-effective, and non-invasive approach to optimize thyroid cancer diagnosis.[9]

Inflammation is a protective process that occurs in organisms as a response to tissue damage. Various types of leukocytes migrate to the site of tissue injury. This migration is mediated by chemotactic and adhesion proteins, including integrins. The first migrating cells are neutrophils, macrophages, and mast cells, all of which secrete Reactive Oxygen Species (ROS), vasoactive molecules such as histamine and leukotrienes, as well as cytokines, chemokines, and proteases that remodel the extracellular matrix. Inflammation is typically an auto-limited process. However, persistent or abnormal inflammation, or failure of anti-inflammatory mechanisms, can result in chronic inflammation.[10]

Leukocytes physiologically secrete ROS and reactive nitrogen species to eliminate pathogens. However, these highly reactive metabolites induce the production of peroxynitrite and other mutagenic agents that can cause DNA damage. Cancer cells release cytokines and chemokines, which support cancer cell growth and recruit leukocytes to the cancer site. Pro-inflammatory cytokines produced by cancer cells play a crucial role in cancer progression.[10]

Systemic inflammation plays an important role in the pathophysiology of cancer. The pathophysiology of the inflammatory response to cancer is marked by increased angiogenesis and DNA damage. Monocytes and lymphocytes work as anti-tumour agents. Low lymphocyte and monocyte counts have been seen in advanced-stage malignancies and are linked to a poor prognosis. Monocytes cause cancer cells to undergo apoptosis in order to decrease angiogenesis, which in turn reduces invasion and the advancement of cancer. Specifically, low lymphocyte levels are associated with immune suppression in cancer patients. Neutrophilia is believed to occur due to paraneoplastic activity from the primary tumour or production of Granulocyte Colony-Stimulating Factor (G-CSF).[11]

In our study, we found a high Neutrophil-Lymphocyte Ratio (NLR $\geq$ 2.4846) in 31 individuals (68.89%), all of whom were diagnosed with papillary thyroid cancer. The lowest NLR was 1.11, the highest was 5.07, with a mean of 2.4846 and a standard deviation of 1.08190. Based on ROC analysis, the AUC for NLR was 0.852 (95% CI: 0.766–0.938) with a p-value < 0.001. This indicates a

significant relationship between NLR levels and the risk of papillary thyroid cancer. Our findings are consistent with the studies conducted by Seretis, Manatakis, Xue Zhang, and Scognamillo.[12–14]

In addition, cancer cells generate inflammatory signals and promote inflammation. Cytokines released by inflammatory cells interact with the bone marrow, which produces neutrophils and lymphocytes. NLR may be an indicator of inflammation because there is compelling evidence linking systemic inflammation to neutrophilia and lymphocytopenia.[15]

Monocytes and lymphocytes act as anti-tumor. Low levels of lymphocytes and monocytes are associated with poor prognosis and have been observed in advanced cancer. Low lymphocytes are associated with suppression of the immune system in patients with cancer. Neutrophilia is thought to occur due to paraneoplastic activity of the primary tumor or production of Granulocyte Colony Stimulating Factor.[12,16]

Seretis et al. found high NLR values (>2.5) in patients with papillary thyroid microcarcinoma (PTMC). The NLR values in benign thyroid nodules and PTMC showed a significant statistical difference (p=0.001).[12] Manatakis studied the diagnostic accuracy of the Neutrophil-Lymphocyte Ratio (NLR) and Platelet-Lymphocyte Ratio (PLR) in detecting occult papillary thyroid microcarcinoma (PTMC) in 397 patients who underwent thyroidectomy between 2007 and 2016. NLR was significantly higher in the papillary thyroid carcinoma and microcarcinoma groups compared to benign lesions (p = 0.026).[13]

Xue Zhang et al. studied 487 thyroid tumour patients, measuring neutrophils (NE), leukocytes, monocytes, lymphocytes, platelets, monocyte/lymphocyte ratio (MLR), NLR, and platelet/lymphocyte ratio (PLR). They found that the serum levels of PLR, NLR, CRP, and IL-27 in thyroid adenoma (TA) and differentiated thyroid carcinoma (DTC) were higher than in the control group.[17]

Scognamillo et al. conducted a retrospective study of 112 patients over five years at the University of Sassari Surgery Department, divided into two groups: 50 patients with papillary thyroid cancer (Group A) and 62 patients with benign thyroid nodules (Group B). They found that the average NLR was significantly higher in the papillary thyroid cancer group compared to the benign thyroid nodule group.[3]

Although promising in terms of sensitivity, the NLR value can be influenced by medical conditions that affect the type count value of leukocytes such as acute infection, viral or bacterial infection, allergic reaction, cardiovascular disease, connective tissue disease, administration of certain medications). Lymphocytopenia can occur due to infections, malnutrition, connective tissue disorders, severe stress, and strenuous physical exercise.[3]

However, when it comes to predicting papillary thyroid cancer, the combination of NLR and TSHs does not work well. Numerous unstudied variables, including NK cells, ROS, NO, IL-6, and IL-37, may have contributed to the pathophysiology of thyroid cancer. This study's weaknesses were a result of its retrospective cross-sectional design.

CONCLUSION

NLR are more potential than TSHs as predictors of papillary thyroid cancer. Therefore, it is recommended to use NLR as a predictor for papillary thyroid cancer.

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DISCLOSURE

No conflict of interest

REFERENCES

1. Monson JR, Weiser MR. Sabiston Textbook of Surgery, 18th ed. The Biological Basis of Modern Surgical Practice. *Dis Colon Rectum*. 2008 Jul;51(7):1154.
2. Tiwari PK, Varghese B, KK Arunjeet, et al. Feasibility of The Use of Neutrophil To Lymphocyte Ratio (NLR) As An Adjunct To Cytology To Suggest Thyroid Malignancy: A Prospective Study [Internet]. 2021. Available from: https://www.researchsquare.com/article/rs-539030/v1
3. Maulana A, Dwi Wibowo M. Description of Neutrophil-Lymphocyte Ratio in Patients with Thyroid Nodules Description Study at Dr Soetomo Hospital Period January 2018 – December 2020. *International Journal of Research Publications*. 2022;100(1):142-167.
4. Kim HK, Yoon JH, Kim SJ, et al. Higher TSH level is a risk factor for differentiated thyroid cancer. *Clin Endocrinol (Oxf)*. 2013;78(3):472–7.
5. Golbert L, de Cristo AP, Faccin CS, et al. Serum TSH levels as a predictor of malignancy in thyroid nodules: A prospective study. *PLoS One*. 2017;12(11):e0188123–e0188123.
6. Fiore E, Rago T, Provenzale MA, et al. Lower levels of TSH are associated with a lower risk of papillary thyroid cancer in patients with thyroid nodular disease: thyroid autonomy may play a protective role. *Endocr Relat Cancer*. 2009;16(4):1251–60.
7. Demircioglu ZG, Demircioglu MK, Aygun N, et al. Relationship Between Thyroid-Stimulating Hormone Level and Aggressive Pathological Features of Papillary Thyroid Cancer. *Sisli Etfal Hastan Tıp Bul*. 2022;56(1):126–31.
8. Petranović Ovčariček P, Verburg FA, Hoffmann M, et al. Higher thyroid hormone levels and cancer. *Eur J Nucl Med Mol Imaging*. 2020;48(3):808–21.
9. Nieto H, Boelaert K. Women In Cancer Thematic Review: Thyroid-stimulating hormone in thyroid cancer: does it matter? *Endocr Relat Cancer*. 2016;23(11):T109–21.
10. Guarino V, Castellone MD, Avilla E, et al. Thyroid cancer and inflammation. *Mol Cell Endocrinol*. 2010;321(1):94–102.
11. Liu J, Du J, Fan J, et al. The Neutrophil-to-Lymphocyte Ratio Correlates with Age in Patients with Papillary Thyroid Carcinoma. *ORL*. 2015;77(2):109–16.
12. Seretis C, Gourgiotis S, Gemenetzis G, et al. The significance of neutrophil/lymphocyte ratio as a possible marker of underlying papillary microcarcinomas in thyroidal goiters: a pilot study. *The American Journal of Surgery*. 2013;205(6):691–6.
13. Manatakis DK, Tseleni-Balafouta S, Tzelves L, et al. Diagnostic Accuracy of Preoperative Neutrophil-to-Lymphocyte and Platelet-to-Lymphocyte Ratios in Detecting Occult Papillary Thyroid Microcarcinomas in Benign Multinodular Goitres. *J Thyroid Res*. 2018;2018:3470429.
14. Mulita F, Verras GI, Dafnomili VD, et al. Thyroidectomy for the Management of

Differentiated Thyroid Carcinoma and their Outcome on Early Postoperative Complications: A 6-year Single-Centre Retrospective Study. *Chirurgia (Bucur)*. 2022;117(5):556.

15. Haider N, Mahmood Z, Khalid F, et al. Neutrophils to lymphocytes ratio between benign and malignant thyroid nodule. *Pak J Med Sci*. 2021;37(7):1908–11.
16. Offi C, Romano RM, Cangiano A, et al. Evaluation of LMR, NLR and PLR as predictors of malignancy in indeterminate thyroid nodules. *Acta Otorhinolaryngol Ital*. 2021;41(6):530–6.
17. Zhang X, Li S, Wang J, et al. Relationship Between Serum Inflammatory Factor Levels and Differentiated Thyroid Carcinoma. *Technol Cancer Res Treat*. 2021;20:1533033821990055–1533033821990055.

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ORIGINAL ARTICLE

Pengaruh Tingkat Keparahan Asidosis Pre-Operatif Terhadap Gejala *Trias of Death* Pasien Trauma Tumpul Abdomen Pasca Laparotomi Eksplorasi di RSUP Prof. dr. I.G.N.G. Ngoerah Denpasar

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ABSTRAK

Tujuan: Mengetahui pengaruh tingkat keparahan asidosis pre-operatif terhadap gejala *trias of death* pada pasien trauma tumpul abdomen pasca dilakukan tindakan laparotomi eksplorasi di RSUP Prof. dr. I.G.N.G. Ngoerah Denpasar**. Metode:** Penelitian analitik kohort retrospektif melibatkan 25 sampel trauma tumpul abdomen dari bulan Januari 2022-Januari 2023. Data pH darah pre dan *post*-laparotomi eksplorasi, INR, suhu tubuh, umur, dan jenis kelamin dikumpulkan dari rekam medis. **Hasil:** Sebanyak 3 (12%) pasien dengan asidosis berat dan 2 (8%) pasien asidosis ringan pre-operatif mengalami gejala *trias of death*. Terdapat hubungan signifikan antara pH pre-operasi dengan gejala *trias of death* (p=0,003). Asidosis berat pre-operasi merupakan faktor risiko gejala *trias of death* pasca operasi (RR=8,3;1,87-33,05). **Simpulan:** keparahan asidosis pre-operatif berpengaruh terhadap gejala *trias of death* pasien trauma tumpul abdomen pasca dilakukan laparotomi eksplorasi.

Kata Kunci: trauma tumpul abdomen, asidosis, *trias of death*.

ABSTRACT

Aim: *to determine the effect of pre-operative acidosis severity on trias of death symptoms in patients with abdominal blunt trauma after exploratory laparotomy at Prof. dr. I.G.N.G. Ngoerah Denpasar Hospital**. Methods:*** *A retrospective cohort analytical study involved 25 samples of abdominal blunt trauma from January 2022-January 2023. Blood pH, INR, body temperature, age, and sex data were collected from medical records.* ***Results:*** *A total of 3 (12%) patients with pre-operative severe acidosis and 2 (8%) patients with mild acidosis experienced trias of death symptoms. There was a significant association between preoperative pH and trias of death symptoms (p=0.003). Preoperative severe acidosis was a risk factor for postoperative trias of death symptoms (RR=8.3;1.87-33.05).* ***Conclusion:*** *The severity of pre-operative acidosis affects the symptoms of trias of death in patients with abdominal blunt trauma after exploratory laparotomy.*

Keywords: *blunt abdominal trauma, acidosis, trias of death*.

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PENDAHULUAN

Trauma tumpul abdomen dapat terjadi pada setiap orang di seluruh dunia dari berbagai usia dan sangat berhubungan dengan tingkat kematian yang tinggi.[1] Terdapat jutaan orang yang mengalami trauma tumpul

abdomen setiap tahunnya dan berbanding lurus dengan peningkatan biaya perawatan di fasilitas kesehatan.[2] Tanda pasien yang berkaitan dengan peningkatan risiko kematian dikenal dengan *trias of death* (TOD) yang terdiri dari hipotermia, koagulopati dan asidosis.[3,4] Insiden pasien trauma yang datang dengan *trias of death* (TOD) rendah, namun berkaitan dengan tingkat mortalitas yang tinggi. Angka kematian tidak berubah meskipun terjadi perbaikan pada sistem trauma dan resusitasi.[5]

Asidosis adalah kondisi peningkatan asam di dalam darah yang dapat disebabkan oleh trauma dan penyakit tertentu.[3,4] Syok hipovolemi yang sering menyertai trauma tumpul abdomen menjadi salah satu pemicu asidosis. Kehilangan darah dalam jumlah besar dapat mengubah metabolisme aerobik menjadi anaerobik sehingga terjadi penumpukan asam laktat.[1] Keadaan asidosis juga akan menghambat fase generasi trombin dan mempercepat degradasi fibrinogen. Hal ini menyebabkan koagulopati sehingga akan meningkatkan angka mortalitas.[3]

Sebagian besar pasien trauma tumpul abdomen datang ke Instalasi Gawat Darurat (IGD) RSUP Prof. dr. I.G.N.G. Ngoerah Denpasar dengan kondisi asidosis sebelum dilakukan pembedahan, bahkan dengan kondisi *trias of death* (TOD). Untuk itu, peneliti ingin mengetahui pengaruh tingkat keparahan asidosis pre-operatif terhadap TOD pada pasien trauma tumpul abdomen pasca dilakukan tindakan laparotomi eksplorasi di RSUP Prof. dr. I.G.N.G. Ngoerah Denpasar.

METODE

Penelitian observasional menggunakan rancangan kohort retrospektif. Pasien trauma tumpul abdomen yang dilakukan laparotomi eksplorasi di RSUP Prof. dr. I.G.N.G. Ngoerah Denpasar pada 1 Januari 2022-31 Januari 2023 diinklusi ke dalam penelitian. Asidosis pre-operatif ditentukan dari nilai pH analisis gas darah pre-operatif yang diklasifikasikan menjadi asidosis ringan (pH 7,20-7,35) dan berat (pH< 7,2). Ada tidaknya gejala TOD (asidosis [<7,35], hipotermia [<36^{o}C], dan koagulopati [INR>1,1]) pasca operasi ditentukan dari catatan dalam rekam medis. Karakteristik dasar pasien seperti umur dan jenis kelamin juga dikumpulkan. Analisis data dilakukan dengan uji *chi-square* dengan nilai signifikansi ditetapkan jika p<0,05. Semua analisis data dikerjakan dengan perangkat SPSS 26.0

HASIL

Sebanyak 25 pasien trauma tumpul abdomen diinklusi ke dalam penelitian. Rerata usia pada kelompok dengan gejala TOD adalah 23 (±13,9) tahun, lebih rendah dibandingkan pada kelompok tanpa gejala TOD 27 (±12,1) tahun.

Sebanyak 3 (12%) pasien asidosis berat pre-operatif mengalami gejala TOD, sedangkan hanya 2 (8%) pasien asidosis ringan yang mengalami TOD pasca operasi sebanyak 2 pasien (8%). Perbedaan ini signifikan secara statisik dengan nilai p=0,003. (**Tabel 1**). Asidosis berat merupakan faktor risiko TOD, dimana meningkatkan risiko sebesar 8,3 kali lebih tinggi dibandingkan asidosis ringan (interval kepercayaan [IK] 95%=1,87-33,05).

Rerata usia pasien asisodis berat (21,5±13,5 tahun) lebih rendah dibandingkan dengan asidosis ringan (27,3±12,1 tahun). Mayoritas sampel adalah laki-laki dan hanya 1 sampel perempuan. Usia dan jenis kelamin tidak berpengaruh signifikan terhadap kejadian asidosis pre-operatif (**Tabel 2**).

Tabel 1. Pengaruh Asidosis Pre-Operasi Terhadap *Trias of Death* Pada Pasien Trauma Tumpul Abdomen

pH Pre-Operasi (n,%)	*Trias of Death*		RR	IK 95%	p
	Ya	Tidak			
Asidosis berat	3 (12%)	1 (4%)	8,3	1,87-33,05	0,003
Asidosis ringan	2 (8%)	19 (76%)			

Tabel 2. Faktor yang Berhubungan dengan Asidosis Pre-Operatif

Karakteristik	Asidosis preoperasi		p
	Asidosis berat	Asidosis ringan	
Umur (rerata ± SD)	21,5±13,5	27,3±12,1	0,661
Jenis kelamin (n, %)			
Laki-laki	4 (16%)	20 (80%)	0,656
Perempuan	0 (0%)	1 (4%)	

DISKUSI

Trauma tumpul abdomen sering dialami oleh usia produktif karena lebih banyak beraktivitas di luar rumah dan berkaitan dengan kecelakaan lalu lintas. Hal ini sesuai dengan hasil penelitian yang menunjukkan rerata pasien berada dalam usia 20-an tahun, meskipun tidak ditemukan pengaruh usia terhadap gejala TOD. Rerata usia ini bervariasi pada beberapa penelitian sebelumnya. Muthukumar dkk.[6] melaporkan bahwa rerata usia pasien dengan TOD adalah 42,3 tahun. Penelitian Panchal dkk.[7] melaporkan rerata umur pasien trauma tumpul abdomen adalah 35 tahun.

Jenis kelamin laki-laki juga dikaitkan dengan kejadian trauma tumpul abdomen yang lebih tinggi, namun tidak ada perbedaan kejadian TOD berdasarkan jenis kelamin. Laki-laki dilaporkan lebih banyak mengalami TOD, namun tidak berbeda bermakna dibandingkan dengan perempuan.[6,8] Penelitian Mitra dkk.[5] melaporkan bahwa proporsi laki-laki lebih banyak dengan kondisi tidak selamat, meskipun tidak signifikan berkaitan dengan mortalitas.

Asidosis adalah gangguan keseimbangan asam basa di dalam darah sehingga menyebabkan pH darah turun (pH<7,35).[9] Jenis asidosis yang terjadi pada kasus trauma adalah asidosis metabolik akibat perubahan metabolisme pada tingkat selular. Metabolisme normal dilakukan secara aerobik, namun pada kasus trauma dengan perdarahan yang masif terjadi metabolisme anaerob akibat kurangnya perfusi oksigen. Metabolisme anaerob tersebut menyebabkan penumpukan asam laktat yang menggeser pH dalam darah.[10]

Penelitian ini menunjukkan bahwa asidosis berat pre-operatif meningkatkan risiko TOD pasca laparotomi eksplorasi sebesar 8,3 kali lebih besar dibanding asidosis ringan. Berbagai penelitian sebelumnya juga melaporkan bahwa derajat asidosis berkaitan dengan TOD. Rerata pH pasien dengan TOD lebih rendah dibandingkan dengan kelompok tidak TOD.[6] Andila dkk.[11] melaporkan hubungan antara keparahan asidosis pre-operatif dengan mortalitas pada pasien trauma abdomen yang dilakukan eksplorasi laparotomi. Penelitian lain oleh Mitra dkk.[5] menemukan adanya perbedaan rerata pH antara kelompok yang meninggal dan tidak.

Syok merupakan salah satu komplikasi pada trauma tumpul abdomen yang dapat

menganggu keseimbangan asam basa tubuh melalui perubahan metabolisme. Gangguan metabolisme ini terjadi karena penurunan aliran darah dalam mikrosirkulasi atau kadar oksigen dalam darah menurun atau kombinasi keduanya. Kondisi ini menyebabkan perubahan adenosine difosfat (ADP) menjadi adenosis trifosfat (ATP) melalui glikolisis anaerobik. Produk akhir glikolisis, piruvat, akan diubah menjadi laktat. Perbandingan laktat terhadap piruvat merupakan indikator hipoksia seluler yang baik.[12,13]

Proses glikolisis anaerob juga melepakan proton berupa ion hidrogen yang terakumulasi sehingga mengurangi *buffer* dari bikarbonat. Dalam keadaan aerob, laktat diangkut dari perifer ke hati untuk dikonversi menjadi CO_2 yang diekskresi melalui pernafasan. Asam laktat akan mengalami akumulasi pada kondisi anaerob yang menimbulkan asidosis laktat. Asidosis laktat terjadi dengan cepat dan dapat dideteksi dengan pemeriksaan analisa gas darah. Kadar laktat merupakan penanda kuantitatif dari beratnya syok.[12,13]

Peran asidosis metabolik pada TOD sangat kompleks. Gejala TOD akan muncul apabila tidak dilakukan resusitasi yang adekuat sehingga menyebabkan *impending organ failure.* Asidosis metabolik ringan dapat terjadi pada pasien dengan penurunan aliran oksigen dan akan berkelanjutan menjadi asidosis berat pada pasien syok.[4]

Keadaan asidosis juga menyebabkan generasi thrombin dan mempercepat degradasi fibrinogen yang nantinya berperan menimbulkan koagulopati.[10] Beberapa penelitian mengkonfirmasi adanya penurunan aktivitas faktor koagulasi pada penurunan pH 7,4 menjadi 7,0.[14] Hasil penelitian juga ditemukan ada hubungan yang signifikan antara koagulopati dengan TOD. Koagulopati mempengaruhi kemungkinan pasien yang mengalami infeksi pada 24 jam pertama pasca trauma karena efek hiperinflamasi dari hipoksia jaringan.[15] Koagulopati pada pasien trauma bersifat kompleks, bisa dalam bentuk koagulopati terkait dilusi atau trauma.[16]

Hemodilusi akibat pemberian cairan intravena selama resusitasi dapat menyebabkan koagulopati dilusi. Koagulopati dilusi terjadi sekitar 70% pasien yang menerima cairan intravena >4 liter.[17] Koagulopati terkait trauma dilaporkan terjadi akibat aktivasi langsung jalur protein C melalui cedera jaringan dan hipoperfusi.[18] Protein C yang aktif akan menghambat faktor koagulasi V dan VIII, sehingga mencegah koagulasi dan meningkatkan fibrinolisis.[14]

Kondisi hipotermia juga mempengaruhi mempengaruhi kemampuan tubuh untuk mengaktifkan kaskade pembekuan. Hipotermia menekan sumsum tulang dan sekuestrasi splenohepatik sehingga menurunkan produksi trombosit dan leukosit yang berperan dalam pembekuan darah. Leukopenia dan trombositopenia menurun ketika pasien dihangatkan.[19] Penelitian ini merupakan penelitian kohort retrospektif dengan jumlah sampel kecil yang disebabkan terbatasnya jumlah kasus yang diamati. Hal ini menyebabkan masih adanya risiko bias dalam penarikan kesimpulan dan analisis data.

SIMPULAN

Tingkat keparahan asidosis pre-operatif berpengaruh signifikan terhadap *trias of death* pada penderita trauma tumpul abdomen pasca dilakukan laparotomi eksplorasi. Umur dan jenis kelamin tidak berpengaruh dengan *trias of death* pada pasien trauma tumpul abdomen.

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DAFTAR PUSTAKA

1. Régnier MA, Raux M, Le YM, Asencio Y, Gaillard J, Devilliers C, dkk. Prognostic significance of blood lactate and lactate clearance in trauma patients. *Anesthesiology*. 2012;117:1276–88.
2. O'Rourke, M.C., Landis, R., Burns, B. Blunt Abdominal Trauma, StatPearls [Internet]. *StatPearls Publishing*. 2022.
3. Corwin GS, Sexton KW, Beck WC, Taylor JR, Bhavaraju A, Davis B, dkk. Characterization of Acidosis in Trauma Patient. *J Emerg Trauma Shock*. 2020;13:213–8.
4. Thorsen K, Ringdal KG, Strand K, Søreide E, Hagemo J, Søreide K. Clinical and cellular effects of hypothermia, acidosis and coagulopathy in major injury. *Br J Surg*. 2011;98:894–907.
5. Mitra B, Tullio F, Cameron PA, Fitzgerald M. Trauma patients with the 'triad of death'. *Emerg Med J*. 2012;29(8):622-5.
6. Muthukumar MV, Karki D, Jatin B. Concept of Lethal Triad in Critical Care of Severe Burn Injury. *Indian J Crit Care Med*. 2019;23(5):206-9.
7. Panchal HA, Ramanuj AM. The study of abdominal trauma: patterns of injury, clinical presentation, organ involvement and associated injury. *Int Surg J* 2016;3:1392-8.
8. Tzeng WJ, Tseng HY, Hou TY, Chou SE, Su WT, Hsu SY. From Death Triad to Death Tetrad-The Addition of a Hypotension Component to the Death Triad Improves Mortality Risk Stratification in Trauma Patients: A Retrospective Cohort Study. *Diagnostics (Basel)*. 2022;12(11):2885.
9. Smith H, Kathleen S, Lee H. Acidosis and citrate: provocative interactions. *Annals of Translational Medicine*. 2018;6(18):374.
10. Wiargitha IK. Trias of Death. *Program Pendidikan Dokter Spesialis Ilmu Bedah Universitas Udayana*. 2017.
11. Andila Y. Tingkat Keparahan Asidosis Pre-Operative Mempengaruhi Mortalitas pada Pasien Trauma Abdomen yang Dilakukan Eksplorasi Laparotomi di RSUP H. Adam Malik Medan [Tesis]. *Fakultas Kedokteran Universitas Sumatera Utara*. 2021.
12. Funk GC, Doberer D, Kneidinger N, Lindner G, Holzinger U, Schneeweiss B. Acid-base disturbances in critically ill patients with cirrhosis. *Liver Int*. 2007;27:901–9.
13. Brohi K, Cohen MJ, Davenport RA. Acute coagulopathy of trauma: mechanism, identification and effect. *Curr Opin Crit Care*. 2007;13(6):680-5.
14. Kaafarani HMA, Velmahos GC. Damage Control Resuscitation In Trauma. *Scand J Surg*. 2014;103(2):81–8.
15. Giustozzi M, Ehrlinder H, Bongiovanni D, Borovac JA, Guerreiro RA, Gąsecka A, dkk. Coagulopathy and sepsis: Pathophysiology, clinical manifestations and treatment. *Blood Rev*. 2021;50:100864.
16. Tieu BH, Holcomb JB, Schreiber MA. Coagulopathy: its pathophysiology and treatment in the injured patient. *World J Surg*. 2007;31(5):1055-64.
17. Maegele MM, Schöchl H, Cohen MJ. An update on the coagulopathy of trauma. *Shock*. 2014;41 Suppl 1:21-5.
18. Brohi K, Cohen MJ, Ganter MT, Schultz MJ, Levi M, Mackersie RC, dkk. Acute coagulopathy of trauma: hypoperfusion induces systemic anticoagulation and hyperfibrinolysis. *J Trauma*. 2008;64(5):1211-7.

19. Bozorgi F, Mirabi A, Chabra A, Mirabi R, Hosseininejad S, Zaheri H. Mechanisms of Traumatic Injuries in Multiple Trauma Patients. *Int J Med Invest*. 2018;7(2):7-15.

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ORIGINAL ARTICLE
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Karakteristik Penyakit pada Tulang Belakang di Bagian Ilmu Bedah Saraf Rumah Sakit Umum Daerah Arifin Achmad Provinsi Riau Periode Januari 2021-Juni 2023

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ABSTRAK

Tujuan: Penelitian ini bertujuan untuk mengetahui karakteristik penyakit pada tulang belakang di Bagian Ilmu Bedah Saraf RSUD Arifin Achmad Provinsi Riau periode Januari 2021-Juni 2023. **Metode:** Penelitian deskriptif retrospektif dengan metode total sampling dan meneliti data sekunder dari rekam medis. **Hasil:** Terdapat 67 rekam medis pasien dengan penyakit pada tulang belakang di Bagian Ilmu Bedah Saraf RSUD Arifin Achmad dari bulan Januari 2021-Juni 2023 yang memenuhi kriteria inklusi dan eksklusi penelitian. Kelompok usia paling sering mengalami penyakit tulang belakang adalah pasien berusia diatas 60 tahun (20,8%), berjenis kelamin laki-laki (65,6%), dan umumnya tidak bekerja (49,5%). Gejala klinis yang paling sering dirasakan adalah nyeri punggung (37,3%) dan spinal stenosis merupakan diagnosis terbanyak yang ditegakkan (23%). Lokasi lesi umumnya terletak di regio lumbar (41,3%) dan tindakan paling sering diambil adalah laminektomi (58,2%). **Kesimpulan**: Penyakit tulang belakang paling banyak dialami oleh lansia, jenis kelamin laki-laki, dan tidak bekerja.

Kata kunci: nyeri punggung, penyakit tulang belakang, penelitian retrospektif.

ABSTRACT

***Aim**: This study aims to determine the characteristics of spinal disease in the Neurosurgery Department of Arifin Achmad Hospital, Riau Province for the period January 2021-June 2023. **Methods:** Retrospective descriptive research using total sampling methods and secondary data testing from medical records. **Results:** There were 67 medical records of patients with spinal disease in the Neurosurgery Department of Arifin Achmad Hospital for the period January 2021-June 2023 who met the research inclusion and exclusion criteria. The age group that most often experiences spinal disease is patients aged over 60 years (20.8%), male (65.6%), and generally unemployed (49.5%). The most frequently felt clinical symptom was back pain (37.3%) and spinal stenosis was the most frequently diagnosed diagnosis (23%). The location of the lesion is generally located in the lumbar area (41.3%) and the most frequently performed procedure is laminectomy (58.2%). **Conclusion:** The spinal disease most commonly affected by elderly, male, and unemployee.*

***Keywords:** back pain, spinal disease, retrospective research.*

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PENDAHULUAN

Vertebra adalah sekumpulan tulang yang disatukan oleh beberapa artikulasio yang tidak hanya melindungi sumsum tulang belakang, namun juga sebagai pendukung gerak tubuh dan menjaga agar postur tubuh tetap tegak.

Tulang belakang terdiri atas 33 ruas, diantaranya tujuh ruas servikal, dua belas torakal, lima lumbar, lima sakral, dan empat koksigeal. Adanya kelainan pada struktur tersebut akan menimbulkan perubahan secara fisik dan berdampak pada terhambatnya aktifitas sehari-hari. Gejala yang muncul sesuai dengan jenis dan letak kelainan pada tulang. Umumnya, penderita dapat merasakan nyeri pada leher atau punggung, nyeri menjalar, kelemahan, kaku hingga sensasi tertusuk-tusuk pada lengan dan tungkai, disfungsi usus atau kandung kemih, mual muntah, serta bentuk tubuh yang tidak proporsional.[1]

Penyakit pada tulang belakang berdasarkan penyebabnya dapat dibedakan menjadi dua kelompok, yakni akibat peristiwa traumatis dan non-traumatis. Peristiwa traumatis berupa kecelakaan kendaraan bermotor, terjatuh, olahraga, ataupun tindak kekerasan. Sedangkan peristiwa non-traumatis dapat diakibatkan oleh kelainan kongenital, genetik, metabolik, vaskular, infeksi, dan penyakit autoimun.[2,3]

Beberapa penelitian mengenai penyakit pada tulang belakang telah dilakukan di berbagai negara. Penelitian yang di Arab Saudi (2015) yang melibatkan 5.929 pasien, 1.669 pasien (28,1%) diantaranya adalah pasien dengan penyakit tulang belakang. Penyakit paling umum terjadi pada regio

lumbar (53,1%) dan regio servikal (27,1%) dengan gejala utama yang sering dirasakan pasien yaitu nyeri. Gejala nyeri pada leher (60,5%) sering terjadi pada usia <30 tahun. *Spondylosis* dan nyeri punggung bawah banyak terjadi di usia >30 tahun pada wanita (7,8% dan 76,2%) dan pada pria (73,9% dan 3,3%). [4,5]

Penelitian Gede, dkk di Rumah Sakit Umum Fatmawati tahun 2014 mencatat sebanyak 104 kasus, dimana 37 kasus merupakan kasus trauma dan 67 kasus non-trauma. Kecelakaan bermobil dan terjatuh dari ketinggian merupakan sebab traumatik yang paling sering terjadi, sedangkan kasus non-trauma yang menyebabkan kelainan pada tulang belakang adalah infeksi dan neoplasma. Belum ditemukan laporan mengenai karakteristik penyakit pada tulang belakang di Rumah Sakit Umum Daerah Arifin Achmad Provinsi Riau.[6]

Penyakit pada tulang belakang merupakan masalah utama dari segi medis, sosial dan ekonomi karena prevalensi dan insidensi yang terus meningkat. Keterlambatan diagnosis sejak keluhan pertama kali dirasakan dan kurangnya upaya pencegahan.[4]

Hal ini akan berdampak pada sosial maupun ekonomi penderita karena dapat menimbulkan keterbatasan baik sementara ataupun permanen. Komplikasi kesehatan yang dapat muncul adalah artropati sendi neuropatik, spastisitas otot, hipotensi, infeksi saluran napas, gangguan imunitas akibat terganggunya produksi leukosit, gangguan berkemih, kelumpuhan, hingga ulkus dekubitus karena tirah baring yang lama.[7]

Mengingat hingga saat ini, belum terdapat literatur yang membahas topik tersebut di Provinsi Riau, maka penelitian ini bertujuan untuk mengetahui karakteristik penyakit pada tulang belakang periode Januari 2021-Juni 2023 di Bagian Ilmu Bedah Saraf RSUD Arifin Achmad Provinsi Riau.

METODE

Rancangan penelitian ini adalah studi deskriptif retrospektif dan menggunakan metode total sampling dengan meneliti data sekunder dari rekam medis pasien yang memiliki penyakit pada tulang belakang di RSUD Arifin Achmad Provinsi Riau periode Januari 2021-Juni 2023. Sampel diambil berdasarkan kriteria inklusi dan eksklusi.

Kriteria inklusi penelitian ini adalah seluruh rekam medis pasien dengan diagnosis penyakit pada tulang belakang di RSUD Arifin Achmad Pekanbaru sejak Januari 2021 hingga Juni 2023. Kriteria eksklusi penelitian ini yaitu rekam medis pasien yang mengandung data kurang lengkap terkait unsur demografi (usia dan jenis kelamin), serta klinis pasien (gejala klinis neurologis dan segmen tulang belakang yang terlibat)

Variabel penelitian ini adalah kelainan tulang belakang, usia, jenis kelamin, domisili, pekerjaan, gejala klinis, diagnosis, lokasi lesi, dan jenis tindakan. Definisi kelainan tulang belakang adalah segala bentuk kelainan dari segi fungsi maupun morfologi yang menyebabkan pasien datang ke Rumah Sakit. Umur didefinisikan berdasarkan KTP yang didaftarkan dalam rekam medis, dibagi menjadi beberapa kelompok, yakni <30 tahun, 30-39 tahun, 40-49 tahun, 50-59 tahun, dan >60 tahun. Jenis kelamin didefinisikan berdasarkan KTP yang dikategorikan sebagai laki-laki dan perempuan. Pekerjaan adalah bidang yang digeluti seseorang untuk mendapatkan penghasilan. Domisili merupakan kedudukan resmi berupa tempat tinggal, mempunyai hak dan kewajiban sesuai kacamata hukum. Gejala klinis adalah keluhan subjektif yang dirasakan subjek penelitian yang membuatnya datang ke rumah sakit. Diagnosis adalah identifikasi kondisi kesehatan maupun jenis penyakit yang diderita pasien melalui suatu pemeriksaan klinis dan hasil tes medis. Lokasi lesi didefinisikan sebagai letak kelainan yang ditemukan saat pemeriksaan. Sementara jenis tindakan adalah riwayat pengobatan yang dijalani oleh pasien sesuai catatan di rekam medis.

Data penelitian diolah dan dianalisa secara deskriptif, serta disajikan dalam bentuk tabel dan narasi untuk menentukan karakteristik pasien dengan penyakit pada tulang belakang di Bagian Ilmu Bedah Saraf RSUD Arifin Achmad Pekanbaru. Penelitian ini telah mendapatkan persetujuan dari Komite Etik FK UNRI sebelum pengambilan data dilakukan.

HASIL

Terdapat 67 rekam medis yang memenuhi kriteria inklusi dan eksklusi penelitian, dirangkum dalam Tabel 1 dan Tabel 2. Laki-laki lebih banyak mengalami kelainan pada tulang belakang (65,6%) dibanding perempuan (34,4%). Sementara itu, distribusi sampel berdasarkan kelompok usia terbanyak pada kelompok usia >60 tahun (20,8%). Sebagian besar sampel berdomisili di Pekanbaru (47,7%). Pasien dengan status tidak bekerja ditemukan lebih banyak (49,5%) dibanding kelompok pekerjaan lainnya.

Tabel 1. Karakteristik penyakit pada tulang belakang berdasarkan kelompok umur, jenis kelamin, domisili dan pekerjaan

Karakteristik	Jumlah Kasus	Persentase
Kelompok Umur		
0-9 tahun	7	10,44%
10-19 tahun	4	5,97%
20-29 tahun	7	10,44%
30-39 tahun	10	14,92%
40-49 tahun	12	17,91%
50-59 tahun	13	19,40%
>60 tahun	14	20,89%
Jenis Kelamin		
Laki-laki	44	65,67%
Perempuan	23	34,32%
Domisili		
Kabupaten Bengkalis	4	5,97%
Kabupaten Indragiri Hilir	3	4,47%
Kabupaten Indragiri Hulu	2	2,98%
Kabupaten Kampar	4	5,97%
Kabupaten Meranti	0	0%
Kuantan Sengingi	1	1,49%
Kabupaten Pelalawan	0	0%
Kabupaten Rokan Hilir	3	4,47%
Kabupaten Rokan Hulu	3	4,47%
Kabupaten Siak	8	11,94%
Kota Dumai	2	2,98%

Kota Pekanbaru	32	47,76%
Luar Riau	5	7,46%
Pekerjaan		
Tidak bekerja	33	49,52%
Petani	6	8,95%
Pelajar	6	8,95%
Pegawai swasta	17	25,37%
Pegawai negeri	5	7,46%

Spinal stenosis adalah diagnosis yang paling banyak ditegakkan (23%) diikuti dengan diagnosis fraktur vertebra (20%). Gejala klinis yang dirasakan umumnya adalah nyeri punggung (37,3%) dan kelemahan anggota gerak (34,3%). Lokasi kelainan pada tulang belakang berdasarkan segmentasinya didapatkan pada servikal (33,3%), torakal (17,3%), lumbar (41,3%) dan sakral (8%). Tindakan yang paling sering dilakukan adalah laminektomi (58,2%), diikuti konservatif (28,3%) (Tabel 2).

Tabel 2. Karakteristik penyakit pada tulang belakang berdasarkan gejala klinis, diagnosis, lokasi lesi, dan tindakan

Karakteristik	Jumlah Kasus	Persentase
Gejala Klinis		
Nyeri punggung	25	37,31%
Lemah anggota gerak	23	34,32%
Kelumpuhan anggota gerak	6	8,95%
Nyeri leher	11	16,41%
Gangguan BAB dan BAK	2	2,98%
Benjolan pada leher	1	1,49%
Benjolan pada punggung	6	8,95%
Diagnosis		
Fraktur vertebra	18	20,00%
Hernia nucleus pulposus	11	12,22%
Lumbar spina bfida	6	6,66%
Ossification of the posterior longitudinal ligament (OPLL)	1	1,11%
Spinal cord hematoma	1	1,11%
Spinal stenosis	21	23%
Spondilitis non-TB	3	3,33%
Spondilitis TB	10	11,11%
Spondilolistesis	12	13,33%
Lokasi		
Servikal	25	33,33%
Thorakal	13	17,33%
Lumbar	31	41,33%
Sacral	6	8,00%
Tindakan		
Laminektomi	39	58,20%
Posterior Lumbar Interfusion	1	1,49%
Konservatif	19	28,35%
Anterior Cervical Disectomy and Fusion (ACDF)	1	1,49%
Reseksi & rekonstruksi cele	6	8,95%
Laminoplasty	1	1,49%

DISKUSI

Total kelainan pada tulang belakang sejak bulan Januari 2021 – Juni 2023 di divisi Bedah Saraf didapatkan sebanyak 67 kasus, periode tersebut tertinggi pada rentang usia >60 tahun (20,89%). Hal ini sesuai dengan penelitian Roberto pili, dkk (2018) menyatakan bahwa terdapat hubungan antara usia dengan frekuensi terjadinya kelainan pada tulang belakang. Penjelasan dari segi preventif, peningkatan insidensi tersebut berkaitan dengan peningkatan penyebab spesifik yang dapat dicegah, seperti terjatuh atau kecelakaan lainnya[8].

Dari segi aspek jenis kelamin, laki-laki lebih banyak (65,6%) mengalami kelainan tulang belakang dibanding perempuan (34,3%). Meskipun persentase laki-laki lebih tinggi dibanding perempuan, namun penelitian yang dilakukan oleh Ali pada tahun 2015 di Rumah Sakit Universitas Dammam, Arab Saudi menjelaskan bahwa jenis kelamin dan kelainan tulang belakang memiliki nilai hubungan yang lemah.[9]

Status pekerjaan paling banyak yang mengalami kelainan tulang belakang adalah pasien dengan status tidak bekerja (49,5%). Hasil ini sesuai dengan penelitian yang dilakukan oleh Chad, dkk (2021) menemukan bahwa pasien yang tidak bekerja memiliki

kemungkinan mengalami kelainan tulang belakang yang lebih tinggi dibanding pasien yang masih aktif bekerja. Penyebab yang mendasari adalah pasien yang tidak bekerja cenderung pasien berusia tua, memiliki edukasi yang rendah, dan komorbid yang lebih banyak.[10]

Berdasarkan gejala klinis, umumnya pasien memiliki keluhan utama nyeri punggung (37,3%). Hasil ini sesuai dengan penelitian yang dilakukan oleh Filip Raciborski, dkk pada tahun 2016, menunjukkan bahwa nyeri punggung merupakan keluhan paling banyak yang dirasakan pada pasien dengan kelainan tulang belakang. Faktor penyebab utama adalah penuaan dan gaya hidup, serta penundaan pengobatan sejak keluhan awal dirasakan.[7]

Lokasi lesi pada tulang belakang paling banyak terdapat di regio lumbar (41,3%) dan diikuti dengan regio servikal (33,3%). Hasil ini sesuai dengan penelitian yang dilakukan oleh Ali pada tahun 2015 di Arab Saudi yang menyatakan bahwa lumbar (53,1%) dan servikal (27,1%) merupakan lokasi paling sering mengalami kelainan pada tulang belakang.[9]

Diagnosis paling banyak ditegakkan adalah spinal stenosis (23%) dan tindakan yang paling sering diambil adalah laminektomi (58,2%). Hasil tersebut sesuai dengan penelitian yang dilakukan oleh Martin (2023), yang menyatakan bahwa laminektomi merupakan prosedur yang paling sering diambil untuk mendekompresi kanalis spinalis pada kasus spinal stenosis.[11]

SIMPULAN

Penyakit tulang belakang di Bagian Ilmu Bedah Saraf Rumah Sakit Umum Daerah Arifin Achmad Provinsi Riau sejak bulan Januari 2021 hingga Juni 2023 sebagian besar diderita oleh pasien yang berusia diatas 60 tahun, jenis kelamin laki-laki, dan umumnya tidak bekerja. Gejala klinis yang paling sering dirasakan adalah nyeri punggung dan spinal stenosis merupakan diagnosis terbanyak yang ditegakkan. Lokasi lesi umumnya terletak di regio lumbar dan tindakan paling sering diambil adalah laminektomi.

DAFTAR PUSTAKA

1. Whitney E, Alastra AJ. Vertebral Fracture. StatPearls. 2022 [cited 2023 May 22]; Available from: https://www.ncbi.nlm.nih.gov/books/NBK547673/
2. Ropper AE, Ropper AH. Acute Spinal Cord Compression. Longo DL. *New England Journal of Medicine*. 2017;376(14):1358–69.
3. Molinares DM, Gater DR, Daniel S, dkk. Nontraumatic Spinal Cord Injury: Epidemiology, Etiology and Management. *J Pers Med*. 2022; 12(11):1872.
4. Tulaar ABM, Karyana M, Wahyuni LK, dkk. People with Spinal Cord Injury in Indonesia. *Am J Phys Med Rehabil*. 2017;96(2):S74–7.
5. Alshami AM. Prevalence of spinal disorders and their relationships with age and gender. *Saudi Med J*. 2015;36(6):725–30.
6. Gede I, Dinata S, Agung A, dkk. The Overview of Spinal Cord Injury. *Ganesha Medicina Journal*. 2021;1(2):103-113.
7. Raciborski F, Gasik R, Ktak A. Disorders of the spine. A major health and social problem. *Reumatologia*. 2016;54(4):196–200.
8. Pili R, Gaviano L, Pili L, dkk. Ageing, Disability, and Spinal Cord Injury: Some Issues of Analysis. Vol. 2018, *Current Gerontology and Geriatrics Research*. 2018.
9. Alshami AM. Prevalence of spinal disorders and their relationships with age

and gender. *Saudi Med J*. 2015;36(6):725–30.

10. Cook CE, Garcia AN, Shaffrey C, dkk. The influence of unemployment and disability status on clinical outcomes in patients receiving surgery for low back-related disorders: An observational study. *Spine Surg Relat Res*. 2021;5(3):182–8.
11. Medress ZA, Chen YR, Connolly I, dkk. Laminectomy. Minimally Invasive *Spine Surgery Techniques*. 2023;41–5.

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REVIEW ARTICLE

Weight Regain Outcomes in Roux-en-Y Gastric Bypass vs Sleeve Gastrectomy Type of Bariatric Surgery: A Systematic Review and Meta-Analysis of 13591 Participants

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ABSTRACT

Aim: This study aims to investigate weight regain (WR) outcomes following two of the most popular types of bariatric surgery: Roux-en-Y Gastric Bypass (RYGB) and Sleeve Gastrectomy (SG) following substantial weight loss with a minimum 1-year follow-up. **Methods:** We systematically searched English-language full-text literature from Pubmed, Cochrane, Wiley Library, Proquest, SpringerLink, and ScienceDirect databases from January 2013 to September 2023. This study was registered to PROSPERO (Registration ID: CRD42023468904). **Results:** A total of 6 eligible good-quality cohort studies of 13591 patients were included in this meta-analysis. Our findings indicate that RYGB type significantly has less WR events compared to SG type of bariatric surgery, revealing an OR of 0.47 (95% CI: 0.34, 0.65, $I^2 = 80\%$; $p < 0.0001$). This research may be considered when choosing the type of bariatric surgery. **Conclusion:** Our meta-analysis demonstrates that patients undergoing SG type of bariatric surgery are more prone to experience WR in comparison to RYGB type. Further research aimed at identifying associated risk factors would contribute significantly to advance our understanding in this domain.

Keywords: Bariatric surgery, meta-analysis, Roux-en-Y, Sleeve gastrectomy, Weight regain.

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INTRODUCTION

Obesity, a global health challenge, affects over 1.9 billion adults worldwide, with 650 million classified as obese in 2016. At that time, 39% of adults aged 18 and over (39% of men and 40% of women) were struggling with excess weight. It's noteworthy that the prevalence of obesity across the world is becoming more commonplace worldwide.[1]

The abnormal or excessive accumulation of body fat is the hallmark of obesity, a chronic health issue. The Body Mass Index (BMI) is a regularly used metric to classify obesity. Underweight or normal weight is defined as having a BMI below 25 kg/m². Overweight is defined as having a BMI of 25 to less than 30 kg/m², moderate obesity as having a BMI of 30 to less than 35 kg/m², and severe obesity as having a BMI of 35 kg/m² or higher. Obesity increases the risk of metabolic diseases, such as Type 2 Diabetes Mellitus (T2DM) and cardiovascular disease (CVD), necessitating effective interventions.[2]

Bariatric surgery emerges as the most effective long-term solution for severe obesity and associated metabolic issues, surpassing alternatives like physical activity, dietary modification, pharmaceutical interventions, or management of gut microbiota.[2,3] It is recommended for individuals with BMI > 35

kg/m² (regardless of presence, absence, or severity of coexisting health issues) or for T2DM patients with BMI > 30 kg/m² who do not respond to non-surgical methods. Long term data affirm its safety, efficacy, and mortality risk reduction compared to non-surgical interventions.[4]

Among the various bariatric procedures available, Roux-en-Y Gastric Bypass (RYGB) and Sleeve Gastrectomy (SG) are the most widely performed due to their demonstrated efficacy in promoting substantial weight loss and improving metabolic outcomes.[5,6] These two procedures are favoured for their relatively lower complication rates and durability of weight loss compared to other options like adjustable gastric banding or biliopancreatic diversion However, they present unique challenges when it comes to weight regain (WR).[5,6]

In RYGB, the rerouting of the intestines and creation of a small gastric pouch leads to malabsorption and hormonal changes, but nutrient absorption may normalize over time, contributing to WR. SG removes the stomach's fundus, responsible for ghrelin production, thus promoting early satiety, though WR can occur as the remaining stomach expands postoperatively. As these two procedures dominate bariatric surgery, understanding their specific associations with WR is critical to improving long-term outcomes.[7–9]

RYGB involves creating a small gastric pouch and intestinal rerouting. During RYGB, the stomach is partitioned, forming a compact pouch of 20-30 ml volume, anastomosed with the mid-jejunum, redirecting nutrients to bypass a significant portion of the stomach, duodenum, and the proximal jejunum. SG entails removing 75% of the stomach, forming a tubular-shaped new stomach by transecting along the greater curvature and removing the fundus and body, therefore gastric contents can pass rapidly into the duodenum.[10,11]

While bariatric surgery has gained traction, the number of procedures and patient monitoring continues to rise. Weight regains has emerged as a significant concern for bariatric surgeons. The need for revisional surgery due to weight loss failure, is a challenging and risky procedure, which also increasing.[12] Reports suggest that 15% to 35% of bariatric surgery patients fail to achieve their weight loss goal.[3] Despite being the most effective approach for obesity, weight regain (WR) after surgery remains burdensome. In research involving 300 individuals who underwent Roux-en-Y gastric bypass (RYGB), it was found that 37% experienced substantial weight regain when assessed seven years later. Another analysis, through a systematic review, indicated that as many as 76% of Sleeve Gastrectomy (SG) patients encountered notable weight regain after a six-year follow-up period.[13]

Another research indicates significant variations in the occurrence of weight regain within the bariatric population. According to the Longitudinal Assessment of Bariatric Surgery study (LABS), the average weight regain is approximately 4% for individuals who undergo RYGB within 3 to 7 years post-surgery. Conversely, studies from Sweden and the Netherlands suggest higher figures, reporting that 20 to 24% of patients have gained more than 15% of their body weight five years after undergoing RYGB or SG.[14] The variability in WR rates can be partly attributed to the lack of consensus on the definition of WR, as it varies significantly between studies. This inconsistency in WR definitions, along with differences in study populations and follow-up durations, contributes to the challenges in assessing long-term outcomes of RYGB and SG.[5,6,15–18]

Although WR incidence following bariatric surgery has been thoroughly documented in recent years, few systematic reviews and meta-analyses focus specifically on RYGB and SG. Given the unique mechanisms and the high prevalence of these procedures, a comprehensive understanding of WR in this context is crucial. Therefore, this study aims to provide a thorough summary and ascertain WR outcomes in patients who undergo RYGB and SG after achieving sufficient weight loss, with a minimum of one year of follow-up.

METHODS

Protocol and Registration

Our study of systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines, which offer a standardized framework for the systematic conduct and transparent reporting of studies (**Figure 1**).[19] Prior to the study starting, a meta-analysis protocol was created and prospectively registered in the PROSPERO international database of systematic reviews (Registration ID: CRD42023468904). PROSPERO registration reduces the possibility of reporting bias and improves transparency.[20]

Search Strategy

We systematically searched Pubmed, Cochrane, Wiley Library, Proquest, SpringerLink, and ScienceDirect databases from September 2013 up to September 2023 in English to identify potential research papers. Relevant articles were identified using the following terms: “weight regain” or “obesity relapse” or “obesity recrudescence” or “obesity recurrence” and “bariatric surgery” or “Roux-en-Y” or “gastrectomy” or “metabolic surgery” not “cancer”. We supplemented this search with a hand search of a reference list of relevant articles.

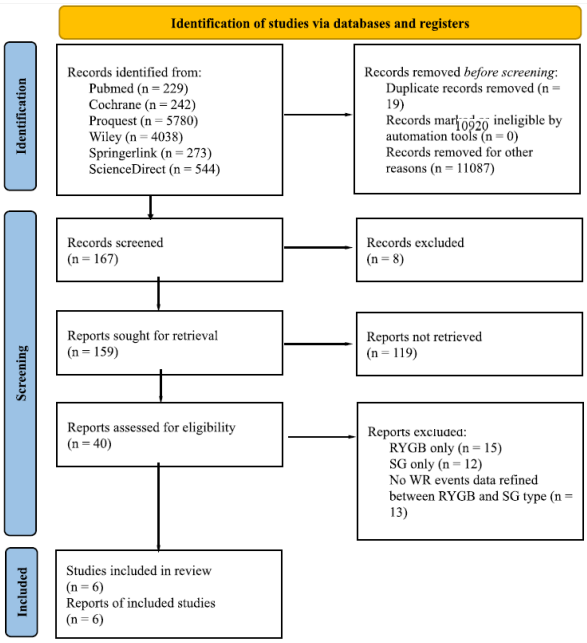

Figure 1. PRISMA flow chart.

Study Selection

Six reviewers (A.A.S.P., E.N.H., J.A., J.G.W., S., and Y.L.I.) independently assessed every study retrieved for inclusion, and disagreements were resolved through consensus. Studies would be included if they met the inclusion criteria as follows: (1) The participants were obese adult patients who received any type of bariatric surgery (minimum 1 year prior) (2) Randomized Controlled Trials (RCTs) and both prospective and retrospective observational studies. (3) Full-text versions accessible. (4) Studies published in English-language. (5) Studies published between January 2013 and September 2023. (6) Studies provide data regarding the events of WR or percentage data following RYGB and SG.

We excluded certain types of studies as follows: (1) Review articles, including systematic reviews, meta-analyses, scoping reviews, and literature reviews. (2) Case reports, protocols, retracted articles, gray

literature, and letters to editors. (3) Studies lacking accessible full-text versions. (4) Research involving non-human subjects and pediatric participants is not within the scope of this analysis. (5) Studies that don't report data related to the events of WR post-RYGB and SG.

Initially, a total of 167 papers were retrieved through these sources. After eliminating duplicate entries and conducting a thorough review of titles and abstracts, 127 papers were excluded from further consideration based on predefined exclusion criteria.

Subsequently, 40 papers underwent a more detailed evaluation, during which we applied inclusion and exclusion criteria to assess their eligibility. Following this comprehensive assessment, we identified 6 studies that met the eligibility criteria and were included for synthesis in this study. These 6 studies collectively involved 13591 patients who participated in various studies conducted across five different countries (Netherlands, Saudi Arabia, India, Iran, and Spain). These studies aimed to investigate the events of WR after RYGB vs SG.

Furthermore, in a study with multiple definitions of WR, the author opted for the definition that exhibited the highest frequency of WR events. The selected definitions are described in **Table 1.**

Data Extraction

Five investigators (A.A.S.P., E.N.H., J.A., J.G.W., and S.) carried out the data extraction process independently using a standardized data collection form. The following items were extracted from each article: first author's name, year of publication, study design, country of study, number of samples in each surgery type, age, gender, surgery indication, type of primary surgery, WR definition in each study, WR outcome including the number or percentage of the population, percentage of the WR, post-operative follow-up time, mean BMI nadir, weight nadir, mean BMI follow-up, and mean weight follow-up.

Quality Assessment

Risk of bias assessment of cohort studies was carried out by two authors (J.G.W and A.A.S.P.) using the modified Newcastle-Ottawa Scale (NOS) and is visually presented in **Table 2.** Discrepancies were resolved through consensus. Using the star system of modified NOS (range 0-9 stars), six studies reviewed.[5,6,15–18] had seven or more stars and were categorized as good quality.

Statistical Analysis

Two investigators (A.A.S.P. and M.I.A.R.) conducted the meta-analysis using Cochrane Review Manager 5.4.1 software. For dichotomous variables, we assessed the outcomes by calculating odds ratios (ORs) along with 95% confidence intervals (CIs). A significance level of $P < 0.05$ was established for statistical significance. To assess heterogeneity among the included studies, we utilized the Tau^2 and Chi^2 heterogeneity test and quantified it using the I^2 statistic. When I^2 was found to be less than 50%, we considered the level of heterogeneity acceptable and applied the fixed-effect model for our analysis.

However, in cases where I^2 exceeded 50%, indicating a high degree of heterogeneity, we opted for the random-effects model to account for this variability. To assess the potential presence of publication bias, we visually represented the data through the utilization of a funnel plot. Funnel plot is a graphical method used to investigate the possibility of publication bias or other biases in the data. The funnel plot typically displays the effect size or standardized effect size (mean difference or odds ratio) of each study

on the horizontal axis and a measure of study precision (standard error or sample size). In an ideal situation with no publication bias, the plot resembles a symmetrical inverted funnel shape. However, if publication bias or other biases are present, the funnel plot may show asymmetry. This asymmetry may manifest as a gap in the plot's lower part, where small studies with non-significant or negative results may be missing.[21]

RESULTS

Characteristics of Studies and Patients

Our search strategy identified 167 potential references. After applying the inclusion criteria, we included 6 cohorts in the meta-analysis, excluding 161 papers (**Table 1**). The eligible studies, spanning from 2015 to 2023, encompassed a total of 13,591 patients (RYGB/SG: 6,415/7,176), among whom 2,723 experienced weight regain events. The incidence rate from these 6 studies was calculated at 20.00% (2,723/13,591).

Participants' mean age at the time of follow-up was 40.53 ± 11.14 years.[5,6,15–18]. The follow-up period ranged from 48 to 84 months post-surgery for all participants.[5,6,15–18] Additionally, the mean pre-operative BMI across the 6 studies was 50.18 ± 8.78 kg/m^2.[5,6,15–18]

Outcomes

In the examination of weight regain events across six studies comparing the effects of RYGB and SG, a statistically significant discrepancy in the likelihood of weight regain emerges between these two surgical approaches. Our meta-analysis strongly favours RYGB over SG, with an odds ratio (OR) of 0.47 (95% CI: 0.34-0.65) (**Figure 2**). This outcome underscores the efficacy of RYGB in mitigating the risk of WR following bariatric surgery. This finding aligns with %WR in each included study despite varied WR definitions across studies, with %WR range of 14.16% to 41.98% in SG type and 8.47% to 35.95% in RYGB type (**Table 2**). But it is also crucial to acknowledge the substantial heterogeneity evident in our analysis, as indicated by an I² value of 81%.

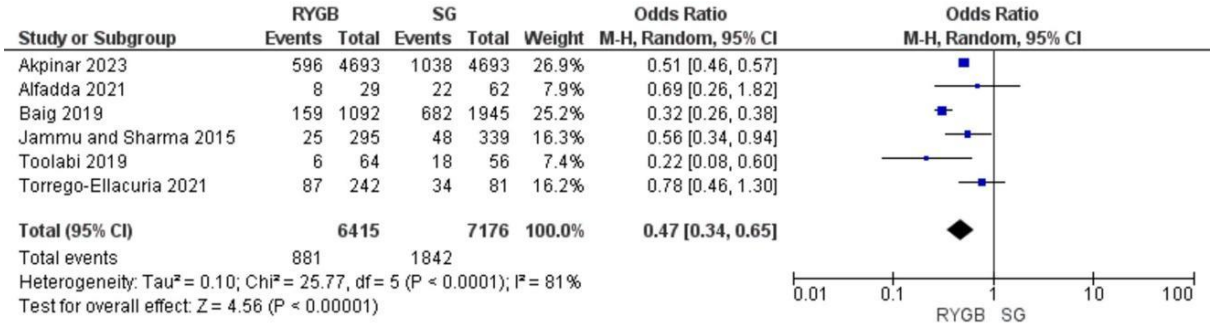

Figure 2. Subgroup analysis for WR on the comparison of RYGB and SG.

Table 1. Characteristics of the included studies.

Study (year)	Country	Design	SG				RYGB				Total				Follow-up (years)
			Patients (n)	Age (mean ± SD)	Pre-op BMI (kg/m^2 ± SD)	WR Event (n)	Patients (n)	Age (mean ± SD)	Pre-op BMI (kg/m^2 ± SD)	WR Event (n)	Patients (n)	Age (mean ± SD)	Pre-op BMI (kg/m^2 ± SD)	WR Event (n)	
Akpinar et al., [15]	Netherlands	Retrospective cohort	4693	42.11 ± 12.29	42.11 ± 12.29	1038	4693	42.46 ± 11.14	45.08 ± 5.61	596	9386	N/A	N/A	1634	5
Alfadda et al. [5]	Saudi Arabia	Prospective cohort	62	N/A	N/A	22	29	N/A	N/A	8	91	33.3 ± 9.7	49.7 ± 9.9	30	6
Baig et al. [6]	India	Prospective cohort	1945	40.62 ± 12.17	116.20 ± 24.82	682	1092	43.98 ± 11.65	120.79 ± 23.29	159	3037	N/A	N/A	841	5
Jammu and Sharma [16]	India	Retrospective cohort	339	23 (no SD data)	35 (no SD data)	48	295	38 (no SD data)	42.5 (no SD data)	25	634	N/A	N/A	73	7
Toolabi et al. [17]	Iran	Retrospective cohort	56	36.6 ± 10.9	40.0 ± 5.8	18	64	36.9 ± 11.5	47.0 ± 7.3	6	120	36.8 ± 11.3	43.2 ± 7.1	24	5
Torrego-Ellacuria et al. [18]	Spain	Retrospective cohort	81	40.36 ± 13.98	43.54 ± 6.88	34	242	45.15 ± 10.65	44.73 ± 6.30	87	323	44.78 ± 11.94	44.94 ± 6.88	121	4

SG = Sleeve Gastrectomy, RYGB = Roux-en-Y Gastric Bypass, BMI = Body Mass Index, SD = Standard Deviation

Table 2. Weight regain definitions.

Study	Weight Regain Definition	Calculation	%WR
Akpinar et al [10]	Increase of ≥ 10% of %WR from the nadir at 2 to 5 year follow-up	(EWL at nadir - EWL at min. FU2) ≥ 10	SG 22.12%; RYGB 12.70%; Total 17.41%
Alfadda et al [11]	Increase of ≥ 25% of %WR from the nadir at min. 1 year follow-up	(EWL at nadir - EWL at min. FU1) ≥ 25	SG 35.48%; RYGB 27.59%; Total 32.97%
Baig et al [12]	Increase of ≥ 25% of %WR from the nadir at 5 year follow-up	(EWL at nadir - EWL at FU5) > 25	SG 35.06%; RYGB 14.56%; Total 27.69%
Jammu and Sharma [13]	Any increase in EWL from nadir	(EWL at nadir - EWL at FU7) > 0	SG 14.16%; RYGB 8.47%; Total 11.51%
Toolabi et al [14]	(I) Increase of ≥ 25% of %WR from the nadir at 1 year post-op, or (II) Weight regain more than 10 kg from the weight at 1 year after surgery	(I) (EWL at nadir - EWL at min. FU1) > 25 (II) (Total body weight in kg at min. FU1 - Total body weight in kg at nadir) > 10	SG 32.14%; RYGB 9.38%; Total 20%
Torrego-ellacuri et al [15]	Any increase in kilograms from nadir	(Total body weight in kg at FU4 - Total body weight in kg at nadir) > 0	SG 41.98%; RYGB 35.95%; Total 37.46% Range %WR: SG: 14.16% - 41.98% RYGB: 8.47% - 35.95%

EWL = excess weight loss, %WR = percent weight regain, BMI = body mass index, nadir = lowest weight measured after surgery, FU = year follow-up

Publication Bias

To evaluate the possibility of publication bias (**Table 3**), we employed a funnel plot (**Figure 3**). Notably, the funnel plot exhibited asymmetry, which could suggest the presence of publication bias. Nevertheless, it is crucial to exercise caution in interpreting this finding, given that the analysis relies on a relatively limited number of studies, and several factors may contribute to the observed funnel plot asymmetry, including variations in study methodologies.

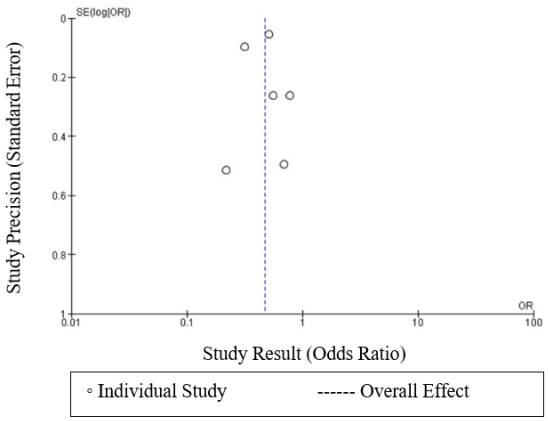

Figure 3. Funnel plots for the publication bias in the meta-analysis for WR on the comparison of RYGB and SG.

DISCUSSION

Summary of Evidence

This meta-analysis compares weight regain (WR) in patients who have undergone Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG). Our findings indicate that WR is more likely after SG than RYGB. Each bariatric surgery type exhibits unique patterns contributing to WR. Gastric pouch dilatation, stomal dilatation, and gastro-gastric fistula are known causes of WR after RYGB. Similarly, gastric pouch dilatation also causes WR in SG.[7,22] However, WR is not solely due to surgical failure; lifestyle factors, mental health, and hormonal/ metabolic imbalance also play significant roles.

It seems that the incidence of weight regain is directly proportional to no remission of weight-related comorbidities. Akpinar et al[15] found that WR in SG was higher in the 5-year follow-up, with less often remission of hypertension (44.7% vs 29.4%), dyslipidemia (38.3% vs 19.3%), and obstructive sleep apnea syndrome (54% vs 20.3%) than RYGB. Meanwhile, patients who had WR after SG who managed to maintain ≥20% total weight loss (TWL) from starting weight, showed more comorbidity remission for hypertension (44.7% vs 29.4%), dyslipidemia (38.3% vs 19.3%), and obstructive sleep apnea syndrome (54% vs 20.3%) than those who did not maintain 20%TWL after SG. Whereas Torrego-ellacuri[18] reported a significant difference between type 2 diabetes in SG and RYGB (26.8% vs 29.3%) but no significant difference in hypertension (37.8% vs 48.3%).

Lifestyle factors contributing to WR include dietary non-adherence and physical inactivity. While bariatric surgery initially reduces caloric intake immediately due to the reduced gastric capacity, decreased hunger, and increased satiety; some patients experience a gradual increase in caloric intake leading to WR.[7,22] Intake of excessive calories, snacks, sweets, oils, and fatty food increases the risk of WR. A cross-sectional observational study by Beckman et al found a positive correlation between total energy, processed foods, and WR.[8] Dietary counselling and consistent nutritional follow-up are pivotal for the long-term success of bariatric surgery, alongside physical activity. The American Society for Metabolic and Bariatric Surgery (ASMBS) recommends at least 30 minutes daily physical activity post-bariatric surgery.[23]

Mental health conditions may be an underlying factor for the occurrence of WR in post-bariatric surgery patients, hindering motivation and dietary compliance.

Table 3. Risk of bias assessment.

Study (cohort)	**Selection (Maximum 4 stars)**				**Comparability (Maximum 2 stars)**	**Outcome (Maximum 3 stars)**			**Total**	
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis controlled for con-founders	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts		
Akpinar et al., [15]	*	-	*	*	**	*	*	-	7	Good quality
Alfadda et al. [5]	*	-	*	*	*	*	*	*	8	Good quality
Baig et al. [6]	*	-	*	*	**	*	*	-	7	Good quality
Jammu and Sharma [16]	*	-	*	*	**	*	*	-	7	Good quality
Toolabi et al. [17]	*	-	*	*	**	*	*	*	8	Good quality
Torrego-Ellacuria et al. [18]	*	-	*	*	*	*	*	-	7	Good quality

There are other maladaptive eating behaviours commonly reported in bariatric surgery patients: grazing, loss of control, and night eating. Surgery doesn't alter the neuropsychiatric pathways.[9]

We observed that the hormonal and metabolic changes induced by bariatric surgery differ between RYGB and SG and contribute to WR outcomes. Specifically, RYGB significantly reduces circulating ghrelin levels by removing the stomach's fundus, which is rich in ghrelin-producing cells. In contrast, SG leads to a sustained but lesser reduction in acyl-ghrelin levels. These differences in ghrelin suppression between the two procedures may explain the higher WR observed in SG patients. Furthermore, RYGB is associated with greater increases in Peptide YY (PYY) and glucagon-like peptide 1 (GLP-1) due to anatomical changes, enhancing satiety and decreasing hunger more effectively than SG.[7,23]

The increased nutrient exposure to L cells in the intestines post-RYGB further supports weight maintenance. These hormonal differences are directly related to our meta-analysis findings, which show that the greater metabolic impact of RYGB correlates with a lower incidence of WR compared to SG.[7,23]

Strength and Limitations

To the best of our knowledge, this is the first meta-analysis that reports the WR outcome among individuals following RYGB in comparison to SG type of bariatric surgery. Our study's strength included the large sample sizes from primary bariatric surgery cases (not revisional) in obese adults from diverse countries and backgrounds. This comprehensive approach allows us to provide meaningful insights into the clinical decision-making process regarding surgery type selection.

However, our analysis has several limitations. First, the variability in WR definitions among the included studies results in heterogeneous inclusion criteria, which may have impacted the overall WR event count. Secondly, the meta-analysis is influenced by various confounding factors, such as dietary habits, physical activity, supplements, mental health issues (e.g., binge eating, depression, anxiety), medication use, and the presence of obesity-related comorbidities. These factors may have affected the WR outcomes and contributed to the heterogeneity observed (I^2 = 80%).

We acknowledge that the high heterogeneity suggests variability in study designs, patient populations, and follow-up durations. Certain patient subgroups, such as those with pre-existing metabolic disorders or more significant weight-related comorbidities, may be more prone to WR and contribute to higher heterogeneity. The variability in study design, such as differing follow-up periods or criteria for defining WR, may also explain this heterogeneity. Although the use of a random-effects model accounts for these differences, it is important to note that this model cannot fully eliminate the uncertainty introduced by the variability. Therefore, while our results are valuable for guiding clinical decision-making, they should be interpreted with caution due to the inherent variability.

Recommendations for Clinical Practice

The findings of this investigation have important implications for clinical practice, especially for bariatric surgeons and patients selecting between RYGB and SG. Based on our findings, patients at higher risk of WR (e.g., those with poor dietary habits, low physical activity, or psychological challenges) may benefit more from RYGB due to its superior hormonal and metabolic effects in promoting long-term weight maintenance.

Clinicians should also emphasize the importance of post-surgical lifestyle modifications, including dietary counselling and physical activity, to mitigate WR risk. Patients should be thoroughly informed about the potential for WR, and individualized recommendations should be made based on patient-specific risk factors, such as pre-existing metabolic conditions or psychological health. Regular follow-up and monitoring of dietary habits, mental health, and physical activity post-surgery are crucial in minimizing the risk of WR and improving long-term outcomes.

Future Research Suggestion

Future studies should focus on more homogeneous patient subgroups, considering comorbidities, surgical techniques, and behavioural factors to better understand the mechanisms of WR post-bariatric surgery. Additionally, long-term studies comparing the hormonal and metabolic responses between RYGB and SG will be valuable in refining strategies to minimize WR. Further research should explore interventions targeting hormonal/metabolic pathways to prevent WR and improve long-term outcomes for bariatric patients.

CONCLUSION

In conclusion, our study demonstrates that patients undergoing RYGB bariatric surgery are more prone to experience WR compared to those undergoing SG. Investigating the associated risk factors would further enhance our study in the future.

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DISCLOSURE

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Conflict of Interest

The authors report no conflicts of interest. The authors are responsible for the content and writing of the paper.

REFERENCES

1. World Health Organisation. Obesity and Overweight. WHO. 2021.
2. Yang M, Liu S, Zhang C. The Related Metabolic Diseases and Treatments of Obesity. *Healthcare*. 2022;10(1616):1–21.
3. Cadena-obando D, Ramírez-rentería C, Ferreira-hermosillo A, et al. Are there really any predictive factors for a successful weight loss after bariatric surgery?. *BMC Endocr Disord*. 2020;4:1–8.
4. Eisenberg D, Shikora SA, Aarts E, et al. 2022 American Society of Metabolic and Bariatric Surgery (ASMBS) and International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) Indications for Metabolic and Bariatric Surgery. *Obesity Surgery*. 2023;33:3–14.
5. Alfadda AA, Al-Naami MY, Masood A, et al. Long-term weight outcomes after bariatric surgery: A single center saudi arabian cohort experience. *J Clin Med*. 2021;10(21):4992
6. Baig SJ, Priya P, Mahawar KK, et al. Weight Regain After Bariatric Surgery—A Multicentre Study of 9617 Patients from Indian Bariatric Surgery Outcome Reporting Group. *Obes Surg*. 2019;29(5):1583–92.

7. El Ansari W, Elhag W. Weight Regain and Insufficient Weight Loss After Bariatric Surgery: Definitions, Prevalence, Mechanisms, Predictors, Prevention and Management Strategies, and Knowledge Gaps—a Scoping Review. *Obes Surg*. 2021;31(4):1755.
8. Beckman RM, Costa AJRB, Caetano N, et al. Food Consumption and Weight Recurrence in Patients Undergoing Bariatric Surgery with a Minimum of 2 Years Post-surgery. *Obes Surg*. 2023;33(10):3223-3229.
9. Furtado TDA, Girundi MG, Campolina CDOC, et al. Depressive and Eating Disorders in Patients Post-Bariatric Surgery with Weight Regain: A Descriptive Observational Study. *Arquivos Brasileiros de Cirurgia Digestiva*.2023;36:e1725.
10. Sherman V, Coulter SA. Bariatric Surgery. *Texas Heart Institute Journal*. 2013;40(3):296.
11. Pucci A, Batterham RL. Mechanisms underlying the weight loss effects of RYGB and SG: similar, yet different. *Journal of Endocrinological Investigation*. 2019;42:117–28.
12. Kim EY. Definition, Mechanisms and Predictors of Weight Loss Failure After Bariatric Surgery. *J Metab Bariatr Surg*. 2023;11(2):39–48.
13. Noria SF, Shelby RD, Atkins KD, et al. Weight Regain After Bariatric Surgery: Scope of the Problem, Causes, Prevention, and Treatment. *Current Diabetes Reports*. 2023;23(3):31–42.
14. Tolvanen L, Christenson A, Surkan PJ, et al. Patients' Experiences of Weight Regain After Bariatric Surgery. *Obesity Surgery*. 2022;32(5):1498–507.
15. Akpinar EO, Liem RSL, Nienhuijs SW, et al. Weight recurrence after Sleeve Gastrectomy versus Roux-en-Y gastric bypass: a propensity score matched nationwide analysis. *Surgical Endoscopy*. 2023;37(6):4351–9.
16. Jammu GS, Sharma R. A 7-Year Clinical Audit of 1107 Cases Comparing Sleeve Gastrectomy, Roux-En-Y Gastric Bypass, and Mini-Gastric Bypass, to Determine an Effective and Safe Bariatric and Metabolic Procedure. *Obesity Surgery*. 2015;26(5):926–32.
17. Toolabi K, Sarkardeh M, Vasigh M, et al. Comparison of Laparoscopic Roux-en-Y Gastric Bypass and Laparoscopic Sleeve Gastrectomy on Weight Loss, Weight Regain, and Remission of Comorbidities: A 5 Years of Follow-up Study. *Obesity Surgery*. 2019;30(2):440–5.
18. Torrego-Ellacuría M, Barabash A, Larrad-Sainz A, et al. Weight Regain Outcomes After Bariatric Surgery in the Long-term Follow-up: Role of Preoperative Factors. *Obesity Surgery*. 2021;31(9):3947-3955.
19. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Journal of clinical epidemiology*. 2009; 62(10):1006–12.
20. Chien P, Khan K, Siassakos D. The pros and pros of registration on PROSPERO. *BJOG*. 2012;119:904–5.
21. Sterne JAC, Sutton AJ, Ioannidis JPA, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ*. 2011;343:d4002.
22. Firat O. Weight regain after bariatric surgery. Annals of Laparoscopic and *Endoscopic Surgery*. 2021;6(0):50–50.
23. Maleckas A, Gudaityte R, Petereit R, et al. Weight regain after gastric bypass: etiology and treatment options. *Gland Surgery*. 2016;5(6):61724–61624.

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