High myocardial oxygen demand index as a poor predictor of prolong length of stay in patient with acute ischemic stroke in Indonesia regional referral hospital: A single center study

By Siti Pujiwati Permata Rima

WORD COUNT	3409	TIME SUBMITTED	10-APR-2024 10:11AM
		PAPER ID	108175073

Original Research

High myocardial oxygen demand index as a poor predictor of prolong length of stay in patient with acute ischemic stroke in Indonesia regional referral hospital: A single center study

Siti Pujiwati Permata Rima[1], *Tri Yunis Miko Wahyono*[1]

[1]Epidemiology Department, Faculty of Public Health, University of Indonesia, Jakarta, Indonesia

Corresponding author:

Siti Pujiwati Permata Rima

ABSTRACT

Background:

The double product (DP) acts as an index for myocardial oxygen oxygen demand, derived from the multiplication of Systolic Blood Pressure (SBP) and Pulse Rate (PR). This research aimed to explore the association between high myocardial oxygen demand and extended hospital stays among acute ischemic stroke patients in Indonesia.

Methods: This study was a retrospective cohort study carried out from January 2022 to December 2022 at a regional referral hospital located in Jakarta, Indonesia. Participants were chosen consecutively until the necessary sample size was achieved. Information extracted from medical records encompassed baseline sociodemographic and clinical variables. Univariate and bivariate analyses were perfomed, along with multivariate analysis utilizing cox proportional hazards, to determine the correlation between elevated myocardial oxygen demand index and length of hospital stay (LOS).

Results: A total of 366 patients were included, with a mean age of 60.05 ± 10.41 years, and 60.4% were male. The mean length of hospital stay was 3.4 ± 3.55 days. Bivariate analysis revealed a significant association between high myocardial oxygen demand index (RR 3.184, 95% CI 1.097-9.258, p=0.028), sepsis (RR 1.942, 95% CI 1.024-4.145, p=0.045), and severe anemia (RR 2.610, 95% CI 1.291-1.465, p=0.036) with prolonged length of stay. Multivariate analysis demonstrated that the high myocardial oxygen demand group had a significantly higher association with prolonged length of stay compared to the normal to low myocardial oxygen demand group (RR 2.116, 95% CI , p=0.035) after controlling for sepsis and severe anemia variables.

Conclusions: The high myocardial oxygen demand index is significantly correlated with extended length of stay among patients with acute ischemic stroke, both before and after adjusting for other potential covariates that could impact treatment duration in such patients.
Keywords: high myocardial oxygen demand index, length of stay, acute ischemic stroke

INTRODUCTION

Prolonged length of stay (LOS) is frequently a significant indicator of suboptimal healthcare quality and inefficient utilization of hospital resources (1,2). Extended hospital stays are linked to elevated mortality rates, higher susceptibility to hospital-acquired infections, and unnecessary utilization of hospital beds and other resources (3). Anticipating the duration of hospital stay contributes to resource planning and initiates efforts to improve healthcare quality. Information regarding the duration of hospitalization for patients with ischemic stroke holds particular significance in Indonesia, given that stroke stands as the foremost cause of mortality among the Indonesian population (4). Comprehending the factors that may contribute to prolonged hospital stays in Indonesia can offer valuable insights for the clinical to design inpatient care strategies aimed at lowering mortality rates attributed to nosocomial infections. It also aids in facilitating effective planning for sufficient bed capacity in hospitals(5,6).

The double product (DP) functions as a gauge of myocardial oxygen consumption, computed by multiplying systolic blood pressure (SBP) and pulse rate (PR) (7). Increased systolic blood pressure and pulse rate are predictive factors associated with a heightened risk of mortality and disability within the general population (8–11). A recent study indicates that a high double product (DP) is associated with major adverse cardiovascular events, including all-cause mortality, recurrent myocardial infarction, and stroke among patients diagnosed with acute coronary syndrome (ACS) who performed percutaneous coronary intervention (PCI) (12). Based on the Indonesian Basic Health Research conducted in 2018, it was found that 34.1% of the adult population in Indonesia had hypertension. (13,14).

There is limited information on factors associated with the length of hospital stay among the Indonesian population, particularly regarding the high myocardial oxygen demand index. Insights into the impact of myocardial oxygen demand index on hospital stay duration could improve patient care, inform the management of acute ischemic stroke

patients, and aid in the development of interventions aimed at minimizing hospital stays, such as community care programs and patient follow-up initiatives (15). We assessed the hospitalization length of stay and its the Myocardial Oxygen Demand Index among acute stroke ischemic patients admitted at Indonesia Tertiary Regional Hospital.

METHOD

Study Design:

This retrospective cohort study was conducted between January 2022 and December 2022 at a regional referral hospital located in Jakarta, Indonesia. Data were collected from e-medical records. Approval for the study was obtained from the Pasar Minggu Regional Public Hospital Ethics Committee, permitting the extraction and use of data from the hospital databases.

Study sample

We included data for all patients diagnosed with acute ischemic stroke aged 18 or older who presented to the emergency department (ED). Patient characteristics, including gender, age, blood pressure (BP), heart rate (HR), presence of severe anemia (Hemoglobin <8 g/dL), presence of sepsis, and medical history, including information about hypertension, diabetes mellitus, and kidney failure, were gathered at baseline. The double product was specifically defined as the product of Systolic Blood Pressure (SBP) in millimeters of mercury (mmHg) and heart rate (HR) in beats per minute. We also collected and analyzed data on the length of stay, denoting the number of days admitted, as a count variable.We excluded patients who required resuscitation (including intubation), GCS < 8, patient who suffered hypovolemic, cardiogenic, neurogenic and distributive shock, and had uncompleted documentation of each variables needed.

The independent variable is the double product, where high myocardial oxygen demand is categorized into two groups: DP ≥20,000 and DP <20,000. The dependent variable is the length of stay, which is further divided into prolonged and normal LOS with a cutoff of > 3 days and ≤ 3 days, respectively. The primary data source for this study was the hospital electronic medical record database, supplemented by the follow-up database containing doctors' performance records.

Statistical Analysis:

Categorical variables were expressed as percentages, and chi-square tests were conducted to analyze the catergorical variables. Continuous variables were described using mean and standard deviation. Bivariate models were employed to identify factors influencing the length of stay. In the multivariate analysis, Cox proportional hazards analysis was utilized to estimate the relative risk associated with the double product. Fully adjusted models for the double product included variables that demonstrated statistical significance in the bivariate analysis. The sample size was calculated with a predetermined α value of 5%, and a p-value of 0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 29.0.

RESULT

Baseline characteristics

This study was conducted from January 2022 to December 2022 and included a total of 366 consecutive patients diagnosed with acute ischemic stroke admitted to the emergency department (ED). Table 1 displays the demographic and clinical characteristics of the participants. The average age was 60.05 ± 10.41 years, with males accounting for 60.4% of the cohort. Among the study population, 64.2% presented with systolic blood pressure >140 and/or diastolic blood pressure >90, while 22.1% exhibited tachycardia upon arrival at the ED. Laboratory findings indicated that 1.9% of the total population experienced severe anemia, and 6.8% had kidney failure. During the treatment period, 14.5% of the total sample developed sepsis. Additionally, 48.9% of the participants had hypertension, and 26.8% had a history of diabetes mellitus. The mean length of stay for the entire population was 3.4 ± 3.55 days.

Double products

For the dependent variable, which is the length of stay (LOS), subjects were grouped into a longer length of stay if > 3 days and a normal LOS if the total treatment days were ≤3 days. In the univariate analysis, 9.8% of patients were categorized as having high myocardial oxygen demand (DP >20,000). In the unadjusted model, the high oxygen requirement myocardial group showed a stronger association with prolonged hospital stay compared to the normal to low oxygen requirement myocardial group, with an odds ratio of 3,184 (95% CI 1,097-9,258), p=0.028. (Table 2).

Table 1. Baseline characteristics of the sample

Characteristics	N = 366
Age (years old; mean ± SD)	60.05 ± 10.41
<65	263 (71.5)
≥ 65	103 (28.5)
Gender (*n*; %)	
Male	221 (60.4)
Female	145 (39.6)
Admission blood pressure (mean ± SD)	155.5 ± 32.03
Normotension	130 (35.5)
Hypertension	236 (64.2)
Admission heart rate (mean ± SD)	92.5 ±15.90
Normal heart beat (60-100 bpm)	281 (76.8)
Bradicardia (<60bpm)	4 (1.1)
Tachycardia (>100bpm)	81 (22.1)
Present of anemia gravis	
Yes	7 (1.9)
No	359 (98.1)
Present of sepsis	
Yes	53 (14.5)
No	313 (85.5)
Hipertension history	
Yes	180 (48.9)
No	186 (50.5)
Diabetes mellitus history	
Yes	98 (26.8)
No	266 (72.7)
Kidney failure	
Yes	25 (6.8)
No	343 (93.2)
High myocardial oxygen demand	
Yes	36 (9.8)
No	330 (90.2)

Length of stay (LOS) (mean ± SD)	3.4 ± 3.55

We also conducted bivariate analysis on several covariate factors that could potentially act as confounding variables in this study. Out of the 7 covariates tested, two variables showed statistically significant effects, the presence of sepsis (RR 1.942, 95% CI 1.024-4.145, p=0.045) and severe anemia (RR 2.610, 95% CI 1.291-1.465, p=0.036). Based on these bivariate results, we proceeded with multivariate analysis using a constant Cox regression model. The findings revealed that the high myocardial oxygen demand group had a significantly higher association with prolonged length of stay compared to the normal to low myocardial oxygen demand group (RR 2.116, 95% CI , p=0.035) (shows in table 3) after controlling for sepsis and severe anemia variables.

Table 2. Bivariat analysis of length of stay (LOS)

Characteristics	**Length of Stay > 3 days n (%)**	**Length of Stay ≤3 days n (%)**	**RR (95%CI)**	***p-value***
Age				
>60	70 (21.9)	23 (6.3)	1.388	0.240
51-60	188 (51.4)	75 (20.5)	(0.812-2.37)	
Gender (*n*; %)				
Male	156 (42.6)	65 (17.8)	1.414	0.185
Female	112 (30.6)	33 (9)	(0.871-2.295)	
Present of anemia gravis				
Yes	6 (1.63)	1 (0.27)	2.610	**0.036***
No	261 (71.3)	98 (26.8)	(1.291-1.465)	
Present of sepsis				
Yes	44 (12.5)	9 (2.5)	1.942	**0.045***
No	244 (61.2)	89(24.3)	(1.024-4.145)	
Hipertension history				
Yes	133 (36.3)	47(12.8)	1.069	0.814
No	135 (36.9)	51(13.9)	(0.673-1.699)	
Diabetes mellitus history				
Yes	68 (18.7)	30 (8.2)	1.078	0.349
No	199 (54.7)	67 (70.9)	(0.929-1.251)	

Kidney failure				
Yes	19 (18.3)	6 (1.6)	1.170	1.000
No	249(93.2)	92(25.1)	(0.453-3.021)	
High myocardial oxygen demand				
Yes	32 (8.7)	4(1.1)	3.186	**0.028***
No	236 (64)	94 (25.7)	(1.097-9.258)	

Table 3. Full Adjusted Multivariate Analysis Examining the Relationship Between High Myocardial Oxygen Demand and Length of Stay Using Cox Proportional Hazards.

Variable	**Adjusted RR**	***p-value***
High myocardial oxygen demand	**2.166**	**0.035**
Sepsis	1.890	0.126
Anemia Gravis	0.999	0.391

DISCUSSION

the high myocardial oxygen demand index and the duration of hospitalization in acute ischemic stroke patients. Findings from univariate, bivariate, and multivariate analyses indicate a significant association between elevated myocardial oxygen demand index and prolonged hospital stays among acute ischemic stroke patients. This association persists even after adjusting for potential confounding factors affecting treatment duration. The double product (DP), derived from multiplying systolic blood pressure by heart rate, serves as a index of myocardial oxygen demand and cardiac workload. Its application in medical practice is expanding, and the double product exhibits a stronger correlation with left ventricular mass compared to daily mean blood pressure (16). Research on the double product as a myocardial oxygen demand index is commonly conducted in the field of cardiology to predict outcomes in patients with cardiovascular diseases. However, there is limited research indicating its effects on patients with neurological disorders, and the clinical neuroscience literature on the double product is very limited. As previously known, preserving optimal cardiac function is essential for maintaining adequate cardiac output, which is pivotal for ensuring sufficient cerebral blood flow following neurological injury such as acute ischemic stroke. Increased myocardial workload has the potential to impair cardiac function, reduce cerebral blood flow, and result in unfavorable long-term functional outcomes (17,18).

Research conducted on the Chinese population reveals that elevated myocardial oxygen demand significantly impacts major adverse cardiovascular events in patients with acute coronary syndrome (ACS) before adjustment for heart rate (HR), with a relative risk of 1.41, 95% CI 1.08 to 1.83, p = 0.012 (12). Similarly, findings from a study conducted in Europe utilizing data from the Ludwigshafen Risk and Cardiovascular Health (LURIC) study demonstrate that an increase in the double product (DP) by 1 standard deviation is associated with a 26.1% higher risk of cardiovascular mortality and a 25.7% higher risk of overall mortality (19). In general, the majority of research on the double product suggests its association with unfavorable clinical outcomes in patients with cardiovascular events. However, these findings contrast with a prior study by Rudolph Schutte et al., where results indicate that in the general population, the double product does not provide additional risk stratification beyond systolic blood pressure (SBP) and pulse rate (PR). In their analysis, incorporating both SBP and PR, the predictive significance of the double product diminished for fatal endpoints (P ≥ 0.07), coronary events (P = 0.06), and stroke (P = 0.12). Interestingly, the double product even showed an inverse association with the risk of all cardiovascular and cardiac events (20).

In our study, we observed a significant association between high myocardial oxygen demand (DP ≥20,000) and prolonged length of stay in patients with acute ischemic stroke. This finding aligns with research conducted on the American population using data from the National Trauma Databank (NTDB), a multicenter trauma registry operated by the American College of Surgeons, spanning from 2007 to 2014. This research suggests that adults with severe traumatic brain injury (TBI) exhibit varied myocardial workload (DP >20,000) profiles with a "U-shaped" relationship with mortality, even in the presence of normal blood pressure. Analysis of their data revealed that the highest DP group was associated with a 25% increased risk of mortality compared to the normal RPP group (aRR 1.25, 95% CI: 1.18 – 1.92, p<0.0001) (21).

In our study, we did not observe a significant association between a history of hypertension or diabetes mellitus and the length of stay in patients with acute ischemic stroke. This finding contrasts with previous research, which reported a significant relationship between these medical histories and length of stay (22–25).

STUDY LIMITATION

The first limitation is that this study was exclusively conducted within only one hospital. As there are variations in the characteristics of care offered between the stroke unit and the ward in each hospotal, the length of patient hospital stay (LOS) may be influenced. The second limitation pertains to the exclusion of several variables from the analyses, including genetic factors, body temperature upon admission, hypertension upon admission, treatment administered upon admission, rehabilitation conducted during hospitalization, and cerebral hemorrhage. However, it's important to acknowledge that these variables could potentially influence both the length of stay (LOS) and functional outcomes. Thirdly, as this study is a retrospective observational analysis, it inherently carries limitations in study design, despite the prospective collection and storage of data.

CONCLUSION:

In conclusion, our data suggest that the double product (DP) is associated with prolonged length of stay in acute ischemic patients, both before and after controlling for confounding variables. These findings are novel and indicate the importance of cardiac performance following acute ischemic stroke. Future studies should closely evaluate the biological plausibility of the direct effect of the myocardial oxygen demand index on the clinical outcomes of patients with acute ischemic stroke.

REFERENCES

1. Barisonzo R, Wiedermann W, Unterhuber M, Wiedermann CJ. Length of stay as risk factor for inappropriate hospital days: interaction with patient age and co-morbidity. J Eval Clin Pract [Internet]. 2013 Feb 26;19(1):80–5. Available from: https://onlinelibrary.wiley.com/doi/10.1111/j.1365-2753.2011.01775.x
2. Celik Y, Celik SS, Bulut HD, Khan M, Kisa A. Inappropriate use of hospital beds: a case study of university hospitals in Turkey. World Hosp Health Serv [Internet]. 2001;37(1):6–13, 33–4. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11372258
3. Taye ZW, Abebil YA, Akalu TY, Tessema GM, Taye EB. Incidence and determinants of nosocomial infection among hospital admitted adult chronic disease patients in University of Gondar Comprehensive Specialized Hospital, North–West Ethiopia, 2016–2020. Front Public Health [Internet]. 2023 Feb 24;11. Available from: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1087407/full

4. Venketasubramanian N, Yudiarto FL, Tugasworo D. Stroke Burden and Stroke Services in Indonesia. Cerebrovasc Dis Extra [Internet]. 2022 Mar 21;12(1):53–7. Available from: https://www.karger.com/Article/FullText/524161
5. Vekaria B, Overton C, Wiśniowski A, Ahmad S, Aparicio-Castro A, Curran-Sebastian J, et al. Hospital length of stay for COVID-19 patients: Data-driven methods for forward planning. BMC Infect Dis [Internet]. 2021 Dec 22;21(1):700. Available from: https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-021-06371-6
6. Taye ZW, Abebil YA, Akalu TY, Tessema GM, Taye EB. Incidence and determinants of nosocomial infection among hospital admitted adult chronic disease patients in University of Gondar Comprehensive Specialized Hospital, North-West Ethiopia, 2016-2020. Front Public Health [Internet]. 2023;11:1087407. Available from: http://www.ncbi.nlm.nih.gov/pubmed/36908459
7. Schutte R, Thijs L, Asayama K, Boggia J, Li Y, Hansen TW, et al. Double Product Reflects the Predictive Power of Systolic Pressure in the General Population: Evidence from 9,937 Participants. Am J Hypertens [Internet]. 2013 May 1;26(5):665–72. Available from: https://academic.oup.com/ajh/article/26/5/665/190874
8. Palatini P. Elevated Heart Rate: A “New” Cardiovascular Risk Factor? Prog Cardiovasc Dis [Internet]. 2009 Jul;52(1):1–5. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0033062009000383
9. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. The Lancet [Internet]. 2002 Dec;360(9349):1903–13. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0140673602119118
10. Hanazawa T, Asayama K, Watabe D, Tanabe A, Satoh M, Inoue R, et al. Association Between Amplitude of Seasonal Variation in Self-Measured Home Blood Pressure and Cardiovascular Outcomes: HOMED-BP (Hypertension Objective Treatment Based on Measurement By Electrical Devices of Blood Pressure) Study. J Am Heart Assoc [Internet]. 2018 May 15;7(10). Available from: https://www.ahajournals.org/doi/10.1161/JAHA.117.008509
11. Williams B, Lindholm LH, Sever P. Systolic pressure is all that matters. The Lancet [Internet]. 2008 Jun;371(9631):2219–21. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0140673608608041
12. Xu T, Zhan Y, Lu N, He Z, Su X, Tan X. Double product reflects the association of heart rate with MACEs in acute coronary syndrome patients treated with percutaneous

coronary intervention. BMC Cardiovasc Disord [Internet]. 2017 Dec 2;17(1):284. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29197333

13. Wajngarten M, Silva GS. Hypertension and Stroke: Update on Treatment. Eur Cardiol [Internet]. 2019 Jul;14(2):111–5. Available from: http://www.ncbi.nlm.nih.gov/pubmed/31360232
14. Astutik E, Puspikawati SI, Dewi DMSK, Mandagi AM, Sebayang SK. Prevalence and Risk Factors of High Blood Pressure among Adults in Banyuwangi Coastal Communities, Indonesia. Ethiop J Health Sci [Internet]. 2020 Nov;30(6):941–50. Available from: http://www.ncbi.nlm.nih.gov/pubmed/33883839
15. van Straten A, van der Meulen JHP, van den Bos GAM, Limburg M. Length of Hospital Stay and Discharge Delays in Stroke Patients. Stroke [Internet]. 1997 Jan;28(1):137–40. Available from: https://www.ahajournals.org/doi/10.1161/01.STR.28.1.137
16. Hermida RC, Fernández JR, Ayala DE, Mojón A, Alonso I, Smolensky M. CIRCADIAN RHYTHM OF DOUBLE (RATE-PRESSURE) PRODUCT IN HEALTHY NORMOTENSIVE YOUNG SUBJECTS. Chronobiol Int [Internet]. 2001 Jan 7;18(3):475–89. Available from: http://www.tandfonline.com/doi/full/10.1081/CBI-100103970
17. Meng L, Hou W, Chui J, Han R, Gelb AW. Cardiac Output and Cerebral Blood Flow. Anesthesiology [Internet]. 2015 Nov 1;123(5):1198–208. Available from: https://pubs.asahq.org/anesthesiology/article/123/5/1198/12559/Cardiac-Output-and-Cerebral-Blood-FlowThe
18. Castle-Kirszbaum M, Parkin WG, Goldschlager T, Lewis PM. Cardiac Output and Cerebral Blood Flow: A Systematic Review of Cardio-Cerebral Coupling. J Neurosurg Anesthesiol [Internet]. 2022 Oct;34(4):352–63. Available from: https://journals.lww.com/10.1097/ANA.0000000000000768
19. Yazdani B, Kleber M, Yücel G, Benck U, März W, Krämer B. ASSOCIATION OF PULSE PRESSURE AND DOUBLE PRODUCT WITH CARDIOVASCULAR AND OVERALL MORTALITY IN LURIC. J Hypertens [Internet]. 2019 Jul;37:e227. Available from: http://journals.lww.com/00004872-201907001-00664
20. Schutte R, Thijs L, Asayama K, Boggia J, Li Y, Hansen TW, et al. Double Product Reflects the Predictive Power of Systolic Pressure in the General Population: Evidence from 9,937 Participants. Am J Hypertens [Internet]. 2013 May 1;26(5):665–72. Available from: https://academic.oup.com/ajh/article/26/5/665/190874

21. Krishnamoorthy V, Vavilala MS, Chaikittisilpa N, Rivara FP, Temkin NR, Lele A V., et al. Association of Early Myocardial Workload and Mortality Following Severe Traumatic Brain Injury*. Crit Care Med [Internet]. 2018 Jun;46(6):965–71. Available from: https://journals.lww.com/00003246-201806000-00017
22. MacIntosh BJ, Cohen E, Colby-Milley J, Fang J, Zhou L, Ouk M, et al. Diabetes Mellitus Is Associated With Poor In-Hospital and Long-Term Outcomes in Young and Midlife Stroke Survivors. J Am Heart Assoc [Internet]. 2021 Jul 20;10(14). Available from: https://www.ahajournals.org/doi/10.1161/JAHA.120.019991
23. Yang CC, Bamodu OA, Chan L, Chen JH, Hong CT, Huang YT, et al. Risk factor identification and prediction models for prolonged length of stay in hospital after acute ischemic stroke using artificial neural networks. Front Neurol [Internet]. 2023 Feb 9;14. Available from: https://www.frontiersin.org/articles/10.3389/fneur.2023.1085178/full
24. Sun Y, Toh MPHS. Impact of diabetes mellitus (DM) on the health-care utilization and clinical outcomes of patients with stroke in Singapore. Value in Health [Internet]. 2009;12(SUPPL. 3):S101–5. Available from: http://dx.doi.org/10.1111/j.1524-4733.2009.00639.x
25. Specogna A V., Turin TC, Patten SB, Hill MD. Hospital treatment costs and length of stay associated with hypertension and multimorbidity after hemorrhagic stroke. BMC Neurol [Internet]. 2017 Dec 10;17(1):158. Available from: http://bmcneurol.biomedcentral.com/articles/10.1186/s12883-017-0930-2