

Hubungan Perubahan Pola Terapi Antiplatelet Setelah Restriksi Clopidogrel dengan Kejadian Serebrovaskular Berulang Pada Pasien *Stroke* di RS Bethesda Yogyakarta

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INTISARI

Restriksi penggunaan clopidogrel dalam Formularium Nasional (FORNAS) 2023 yang membatasi durasi terapi hingga 12 bulan berpotensi mengubah pola terapi antiplatelet pada pasien *stroke* iskemik atau *transient ischemic attack* (TIA). Namun, bukti mengenai hubungan perubahan pola terapi antiplatelet setelah restriksi clopidogrel dan kejadian serebrovaskular berulang di Indonesia masih terbatas. Penelitian ini bertujuan menganalisis hubungan antara perubahan pola terapi antiplatelet setelah restriksi clopidogrel dan kejadian serebrovaskular berulang pada pasien *stroke* di RS Bethesda Yogyakarta. Penelitian ini merupakan studi observasional analitik dengan desain kohort retrospektif menggunakan data rekam medis elektronik dan data *dispensing* farmasi periode Juli 2023–Maret 2025. Pasien yang mencapai *time-zero* setelah 12 bulan terapi clopidogrel dosis standar dikelompokkan menjadi clopidogrel dosis standar, clopidogrel dimodifikasi, dan clopidogrel tidak dipertahankan. Analisis dilakukan menggunakan uji Chi-square, Kaplan–Meier dengan uji *Log-rank*, dan regresi *Cox proportional hazards*. Sebanyak 175 pasien memenuhi kriteria penelitian dengan rerata usia $64,06 \pm 9,90$ tahun dan sebagian besar berjenis kelamin laki-laki (64,6%). Pola terapi didominasi kelompok clopidogrel dimodifikasi (56,6%), diikuti clopidogrel tidak dipertahankan (34,3%) dan clopidogrel dosis standar (9,1%). Rerata lama *follow-up* sejak *time-zero* adalah $210,47 \pm 97,74$ hari, dengan 18 kejadian serebrovaskular berulang (10,3%). Analisis *bivariat* tidak menunjukkan hubungan yang bermakna antara perubahan pola terapi antiplatelet dan kejadian serebrovaskular berulang ($p=0,325$). Analisis *Kaplan–Meier* juga tidak menunjukkan perbedaan probabilitas bebas kejadian serebrovaskular berulang (*Log-rank* $p=0,105$). Analisis *multivariat* menunjukkan clopidogrel dimodifikasi (HR=0,12; CI95%: 0,01–1,34; $p=0,085$) dan clopidogrel tidak dipertahankan (HR=0,22; CI95%: 0,02–2,48; $p=0,220$) tidak berbeda bermakna dibandingkan clopidogrel dosis standar. Penerapan restriksi clopidogrel di RS Bethesda Yogyakarta diikuti oleh perubahan pola terapi antiplatelet yang didominasi clopidogrel dimodifikasi. Perubahan pola terapi antiplatelet setelah restriksi clopidogrel tidak berhubungan secara bermakna dengan kejadian serebrovaskular berulang pada pasien *stroke* di RS Bethesda Yogyakarta.

Kata kunci: Formularium Nasional, kejadian serebrovaskular berulang, restriksi clopidogrel, *stroke* iskemik, terapi antiplatelet.

Association Between Changes in Antiplatelet Therapy Patterns Following Clopidogrel Restriction and Recurrent Cerebrovascular Events Among Stroke Patients at Bethesda Hospital Yogyakarta

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ABSTRACT

The restriction on clopidogrel use in the 2023 Indonesian National Formulary (FORNAS), which limits the duration of therapy to 12 months, may alter antiplatelet therapy patterns in patients with ischemic stroke or transient ischemic attack (TIA). However, evidence regarding the association between changes in antiplatelet therapy patterns following clopidogrel restriction and recurrent cerebrovascular events in Indonesia remains limited. This study aimed to analyze the association between changes in antiplatelet therapy patterns following clopidogrel restriction and recurrent cerebrovascular events among stroke patients at Bethesda Hospital Yogyakarta. This analytical observational study employed a retrospective cohort design using electronic medical records and pharmacy dispensing data from July 2023 to March 2025. Patients who reached time-zero after 12 months of standard-dose clopidogrel therapy were classified into three groups: standard-dose clopidogrel, modified clopidogrel, and clopidogrel not maintained. Data were analyzed using the Chi-square test, Kaplan–Meier analysis with the Log-rank test, and Cox proportional hazards regression. A total of 175 patients met the study criteria, with a mean age of 64.06 ± 9.90 years, and most were male (64.6%). The modified clopidogrel group was the most common therapy pattern (56.6%), followed by clopidogrel not maintained (34.3%) and standard-dose clopidogrel (9.1%). The mean follow-up duration from time-zero was 210.47 ± 97.74 days, during which 18 recurrent cerebrovascular events (10.3%) occurred. Bivariate analysis showed no significant association between changes in antiplatelet therapy patterns and recurrent cerebrovascular events ($p=0.325$). Kaplan–Meier analysis also showed no significant difference in recurrent cerebrovascular event-free probability (Log-rank $p=0.105$). Multivariable analysis indicated that modified clopidogrel (HR=0.12; 95% CI: 0.01–1.34; $p=0.085$) and clopidogrel not maintained (HR=0.22; 95% CI: 0.02–2.48; $p=0.220$) did not differ significantly from standard-dose clopidogrel. The implementation of clopidogrel restriction at Bethesda Hospital Yogyakarta was followed by changes in antiplatelet therapy patterns, predominantly involving modified clopidogrel therapy. Changes in antiplatelet therapy patterns following clopidogrel restriction were not significantly associated with recurrent cerebrovascular events among stroke patients at Bethesda Hospital Yogyakarta.

Keywords: antiplatelet therapy, clopidogrel restriction, ischemic stroke, National Formulary, recurrent cerebrovascular events.