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**Research Article**

# *COST EFFECTIVENESS ANALYSIS* BETWEEN ASPIRIN AND CITICOLINE IN STROKE PATIENT IN PROF DR MARGONO SOEKARJO HOSPITAL PURWOKERTO

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## ABSTRACT

Stroke is the third highest cause of death after heart disease and cancer. An appropriate therapy decision is important because it related to many factors such as cost and quality of life. Most of Indonesian physicians' use citicoline and Aspirin for stroke patients. A Cohort Retrospective study was performed to 40 patients with aspirin and 77 patients with citicoline. Secondary data such as cost, length of stay (LoS) was collected from medical records. Furthermore, patient health level was measured by *National Institute of Health Stroke Scale (NIHSS)* which was collected from patient directly. The average of patients' age was 60.59±11.31 years old. The NIHSS showed no significant difference between aspirin (2.58±2.93) and citicoline (3.10±2.90) groups. Otherwise, LoS was different between two groups (*p value 0.000)*. The average of total cost in aspirin group (IDR 2,593,250.00) was lower than citicoline groups (IDR 11,384,210.00) and the differences were statistically siginificant. The Incremental Cost Effectiveness Ratio (ICER) between aspirin compared to citicoline was IDR 16,905,692.31 per quality of life. Aspirin was strongly dominated to citicoline in cost, LoS and NIHSS.

**Key word**: Cost effectiveness analysis, aspirin, citicoline, stroke, NIHSS

## INTRODUCTION

As the third highest cause of death after heart disease and cancer, stroke prevalence has been increase annually. Moreover, stroke is the main cause of inability. The prevalence of stroke was increase from 2.68 to 3.05 per 1,000 hemorrhagic stroke and from 5.58 to 9.36 per 1,000 non-hemorrhagic stroke (DEPKES RI, 2006). A study by Luk *et al.* (2005) stated that most of stroke patient in Hong Kong Hospital were treated with aspirin and clopidogrel. In other study, sixty six percent of stroke patients in Dr Moewardi Hospital Surakarta, were treated with citicoline (Sukemi, 2011). Moreover, another research and clinical trial of citicoline for ischemic stroke patient conclude that citicoline was ineffective for acute stroke patients (Conant and Schauss 2004; Davalos *et al.,* 2012). Albert, (2012) found that citicoline did not improve recovery after moderate to severe acute ischemic stroke. In contrast, a comparison study of aspirin versus aspirin plus clopidogrel for stroke prevention showed that aspirin monotherapy was cost-effective (Coleman *et al.,* 2012). Recently, aspirin has become the drug of choice for stroke management.

The cost of treatment on stroke managements remains high. This is one of the main problems in stroke managements. In the United States, treatment cost for stroke patients was $18.8 billion in 2008, and the burden related to inability and early death was $15.5 billion (CDC, 2012). The objective of this study was to explore the cost-effectiveness of aspirin compared to citicoline on stroke management.

## MATERIAL AND METHODS

A cohort retrospective study was performed to stroke patient who received aspirin (40 patients) and citikolin (77 patients) for drug therapy in 2012. Patients who got both medicines were excluded. Secondary data such as cost, length of stay, medication history were obtained from patient medical records and hospital information systems. Moreover, a quantitative measurement on important factors

of neurologic examination was adopted from *National Institute of Health Stroke Scale* (NIHSS) which is consisting of 13 scales.

Costs are presented as 2013 Indonesian Rupiah. We categorized cost as direct medical cost (consist of administrative, medical devices, surgery, hospitalization, professional fee, laboratorium, medicine, radiodiagnostic, radiotherapy, and blood transfusion) and indirect cost (patient lost of productivity). The indirect cost measured were earning lost of patients salary due to their hospitalization. Incremental cost-effectiveness ratio was calculated by dividing the incremental of total cost by incremental of outcome, such as quality of life and length of stay.

## RESULT AND DISCUSSION

### Patient socio-demographic and other characteristics

From 117 stroke patients which are eligible, 34.19% (40 patients) were treated with aspirin, and citikoline for the other 65.81% (77 patients). There are no difference in patient socio-demographic and other characteristics between aspirin and citicoline group (*p value >0.05*) (Table I).

The average (SD) of stroke patient age in Prof Dr Margono Public Hospital was 60.59 (11.31). This result was differ to the mean of stroke patients' age in US. Fonarow (2010) showed that the average (SD) of patient's age was 71.00 (14.60) years old. This difference might be caused by many factors such as life style, activity and environment between Indonesia and United States of America.

More than half of the stroke patients are male (57.3%) and graduate from elementary school (59.0%). The result was similar to Goldstein (2011) that prevalence of stroke in man was higher than women for hemorrhagic or non-hemorrhagic stroke. All of the patients are married (100.0%) and most of the patients are housewife (30.7%). Most of the aspirin groups are insured by ASKES (37.5%). Otherwise, in citicoline groups, most of the patients weren't having insurance.

### Disease characteristics of stroke patients

The disease characteristics of stroke patients who were hospitalized in Prof Dr Margono Public Hospital were shown in table II. The risk factor characteristic of stroke patient had the same pattern. Commonly, the patient had hypertension (33.3%) for their risk factors. This was similar with stroke patients in the aspirin groups (47.5%) and citicoline groups (26.0%). The constant increases of blood pressure will deteroriate the blood vessels and also increases the rigidity of endothellium, promote clot formation, and aneurism. All of this mechanism is responsible to stroke incidents (Sofwan, 2010). The pattern of the risk factors in stroke patients was similar with previous research which was about 33.3% (Chairangsarit, 2005).

In Indonesia, it is common that a patient want to go home per their request, even when their physician hasn't decided whether they can go home. This condition can be concluded that the patient has not cured/better than previous condition. At this study, the discharge which was requested by the patients was higher at whom received citicoline (3.4%) compared to aspirin (2.5%) and the difference was statistically significant (p value 0.000).

### NIHSS health level examinations and length of stay

NIHSS examination results show the degree of stroke patient's health level. As described in table III, the distribution of Health level on the Aspirin groups was equal to citicoline group (p value 0.283). Most of the patients has health score less than five (59.% for total, 72.5% for Aspirin group, and 53.2% for citicoline group). It means most of stroke patients which is discharge from the hospital will have a good condition after receiving treatment both aspirin and citicoline. The NIHSS predict that patients with score over than 16 are related to death and severe disability (Meyer, 2002). Even the death patient in the citicoline group (27.3%) was higher than that of the aspirin group (15.0%), although the difference was not statistically different (p value 0.283).

The average of NIHSS health score examination between two gropus wasn't statistically different. Even in the citicoline groups (3.10±2.90) was higher than Aspirin groups (2.58 ± 2.93). This indicated that both aspirin and citicoline has good effect related to health conditions to the stroke patients.

Table I: Socio-demographics and other characteristics of the study subjects

| Patient Characteristics | Total (N=117) | Aspirin (N=40) | Citicoline (N=77) | P value |
|---|---|---|---|---|
| **Age (mean±SD)** | 60.59±11.31 | 61.55±9.27 | 60.10±12.27 | 0.514* |
| **Gender (%)** | | | | 0.666** |
| Male | 67 (57.3) | 24 (60.0) | 43 (55.8) | |
| Female | 50 (42.7) | 16 (40.0) | 34 (44.2) | |
| **Marital Status (%)** | | | | |
| Married | 117 (100.0) | 40 (100.0) | 77 (100.00) | |
| Not married | 0 (0.0) | 0 (0.0) | 0 (0.0) | |
| **Educational Status (%)** | | | | 0.764*** |
| Uneducated | 1 (0.9) | 1 (2.5) | 0 (0.0) | |
| Elementary school | 69 (59.0) | 21 (52.5) | 48 (62.3) | |
| High school | 41 (35.0) | 14 (35.0) | 27 (35.1) | |
| Undergraduate | 6 (5.2) | 1 (.5) | 2 (2.6) | |
| **Employment Status (%)** | | | | 0.521*** |
| Labor | 19 (16.2) | 7 (17.5) | 12 (15.6) | |
| Housewife | 36 (30.7) | 11 (27.5) | 25 (32.5) | |
| Civil servant | 7 (6.0) | 4 (10.0) | 3 (3.9) | |
| Retirements | 13 (11.1) | 5 (12.5) | 8 (10.4) | |
| Farmer | 10 (8.5) | 5 (12.5) | 5 (6.5) | |
| Private sector | 17 (14.5) | 7 (17.5) | 10 (13.0) | |
| Unidentified | 15 (12.8) | 1 (2.5) | 14 (18.2) | |
| **Insurance (%)** | | | | 0.558*** |
| ASKES | 32 (27.4) | 15 (37.5) | 17 (22.1) | |
| Jamkesmas | 40 (34.2) | 13 (32.5) | 21 (35.1) | |
| Non-Insurance | 45 (38.5) | 12 (30.0) | 33 (42.9) | |

* T-test; ** Chi-Square; *** Kolmogorov-Smirnov

The NIHSS score of this study was slightly different with previous finding, 3.05±3.32 for aspirin (Gorelick, 2003) and 6.41±7.62 for citicoline (Mittal, 2011). One of the causes of this finding that the outcome (NIHSS Score) was measured approximately 1 year after patients discharged, whereas, the other research was 3 months after discharged.

Patient Length of Stay (LoS) was described on table III. The average of all stroke patients was 5.55 (±4.24) days. Patients in the citicoline groups (7.16±3.57) had longer LoS compared to Aspirin groups (2.45±3.67) and it different statistically (0.000). Based on LoS data, we can conclude that aspirin was better than citicoline. Chang (2002) stated that the average of LoS on stroke patients was 11 days.

**Cost description in stroke patients in Prof Dr Margono public hospital**

Generally, almost all of cost for stroke patient in citicoline group was higher than aspirin group. The total cost of treatment in stroke patient in citicoline group (11,384.21±3,563.29) was higher than Aspirin Group (2,593.25±2,278.00) and this result was statistically different (p value 0.000), if divided into direct and indirect cost, both direct and indirect cost in citicoline group was higher than that of aspirin group.

Several cost was statistically different between two groups (p value <0.05), there are administration cost, surgery, hospitalization, laboratorium, medicine, and lost of productivity. In medicine cost, patients in citicoline groups (1,413.88±1,409.20) spent almost seven times higher than aspirin group

Table II. Disease characteristics of stroke patients

| Disease Characteristics | Total (N=117) | Aspirin (N=40) | Citicoline (N=77) | P value |
|---|---|---|---|---|
| **Risk Factor Disease (%)** | | | | 0.098 |
| Diabetes (DM) | 1 (0.9) | 0 (0.0) | 1 (1.3) | |
| Hypertension (HT) | 39 (33.3) | 19 (47.5) | 20 (26.0) | |
| DM + HT | 3 (2.6) | 2 (5.0) | 1 (1.3) | |
| Unknown | 74 (63.2) | 19 (47.5) | 55 (71.4) | |
| **Discharge State (%)** | | | | 0.000 |
| Patient request | 19 (16.2) | 1 (2.5) | 18 (23.4) | |
| Better | 36 (30.8) | 5 (12.5) | 31 (40.3) | |
| Cured | 2 (1.7) | 0 (0.0) | 2 (2.6) | |
| Outpatients | 27 (23.1) | 27 (67.5) | 0 (0.0) | |
| No information's | 33 (28.2) | 7 (17.5) | 26 (33.8) | |

Tabel III. NIHSS health level examination and length of stay of stroke patients in Prof Dr Margono public hospital

| Parameters | Total (N=117) | Aspirin (N=40) | Citicoline (N=77) | P value |
|---|---|---|---|---|
| **Examination Results (%)** | | | | 0.283 |
| 0 - 5 | 70 (59.8) | 29 (72.5) | 41 (53.2) | |
| 6 – 10 | 20 (17.1) | 5 (12.5) | 15 (19.5) | |
| 11 – 15 | 0 (0.0) | 0 (0.0) | 0 (0.0) | |
| 16 – 20 | 0 (0.0) | 0 (0.0) | 0 (0.0) | |
| >20 | 0 (0.0) | 0 (0.0) | 0 (0.0) | |
| Died | 27 (23.1) | 6 (15.0) | 21 (27.3) | |
| **NIHSS Score (±SD)** | 2.91 ± 2.91 | 2.58 ± 2.93 | 3.10 ± 2.90 | 0.416 |
| **Length of Stay (±SD)** | 5.55 ± 4.24 | 2.45 ± 3.67 | 7.16 ± 3.57 | 0.000 |

(217.39±311.64). Several factor influenced this results such as the price of medicine (IDR 110,00 per tablet for aspirin, IDR 9,167,50 per tablet fro citicoline, and IDR 6,187,00 per ampule for citicoline also). Moreover, the Length of Stay on citicoline groups was longer than Aspirin groups, it will influenced the medicine cost as patients will got the medicine during their stay on the hospital.

**Cost effectiveness analysis of aspirin and citicoline**

Total cost of treatment for citicoline group was 11,384,210.00 and for Aspirin group was 2,593,250.00, furthermore the NIHSS score for citicoline group was 3.10 and for aspirin groups were 2.58. Based on this can be calculated the Incremental Cost Effectiveness Ratio :

$$ICER = \frac{CoC - CoA}{NIHSS\ A - NHISS\ B}$$

For CoC: cost of citicoline; CoA: cost of Aspirin; NIHSS A: NIHSS score on Cicicoline groups; NHISS: NIHSS score on Aspirine groups

$$ICER = \frac{11.384.210,00 - 2.593.250,00}{3.10 - 2.58}$$

$$ICER = \frac{8.790.960,00}{0.52}$$

ICER= IDR. 16.905.692,31

Table IV. Direct medical and indirect non-medical cost (Thousand Rupiah) in stroke patient at Prof Dr Margono hospital.

| Cost of Treatments | Aspirin (N=40) | Citicoline (77) | P value |
|---|---|---|---|
| **Direct Medical Cost** | | | |
| Administration | 4.85 ± 2.29 | 12.48 ± 5.59 | 0.000 |
| Medical Device | 142.91 ± 73.71 | 220.38 ± 219.71 | 0.358 |
| Surgery | 0.00 ± 0.00 | 6,725.00 ± 0.00 | 0.000 |
| Hospitalization | 223.38 ± 603.40 | 1,239.95 ± 919.83 | 0.000 |
| Profesional Fee | 154.78 ± 60.79 | 170.06 ± 89.13 | 0.659 |
| Laboratorium | 505.66 ± 392.21 | 286.03 ± 224.20 | 0.035 |
| Medicine | 217.39 ± 311.64 | 1,413.88 ± 1,409.20 | 0.000 |
| Radiodiagnostics | 563.64 ± 72.94 | 577.87 ± 206.30 | 0.857 |
| Radiotherapy | 25.00 ± 0.00 | 46.42 ± 26.72 | 0.078 |
| Blood Transfussion | 675.00 ± 636.39 | 337.50 ± 159.09 | 0.588 |
| **Indirect non-medical Cost** | | | |
| Lost of Productivity | 80.64 ± 124.63 | 354.64 ± 303.52 | 0.000 |
| **Total** | 2,593.25 ± 2,278.00 | 11,384.21 ± 3,563.29 | 0.000 |

The calculation results was IDR 16.905.692,31 per incremental NIHSS score. The result indicated that aspirin was more cost-effective compared to citicoline for treating stroke patients in Prof Dr Margono Hospital.

Differ with aspirin which is recommended by several guideline (Maarten *et al*., 2012), citicoline was proven ineffective in enhancing stroke therapy (Connant, 2004). Otherwise, citicoline was still prescribed massively in Prof Dr Margono Public Hospital.

## CONCLUSSION

As aspirin give shorter Length of Stay, better Health Status based on NIHSS score and less costly, we conclude that aspirin is cost effective compared to citicoline in treating stroke patients in Prof Dr Margono Hospital.

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