The Efficacy of Telemedicine for Secondary Prevention and Management Among Stroke Survivors: A Systematic Review and Meta-analysis

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Abstract

Stroke has high mortality and high recurrence rate. Telemedicine usage is rapidly growing as a strategy to optimize stroke secondary prevention by managing stroke risk factors. In order to comprehensively assess the impact of telemedicine intervention, an updated review of more outcomes is required. This systematic review and meta-analysis of randomized controlled trials (RCTs) aim to assess the telemedicine effects on systolic blood pressure, diastolic blood pressure, stroke recurrence, and mortality in post-stroke patients. A literature search of RCTs related to telemedicine intervention from PubMed, Science Direct, Scopus, Web of Science, and ProQuest from 2018 to 2022 was included in this study. The quality of the study was evaluated using the Cochrane RoB 2 tool. We presented the pooling analysis of our result in the form of mean difference (MD) and odd ratio (OR) with 95% CI using RevMan 5.4 software. Six trials involving 3,942 patients met the eligibility criteria to conduct the meta-analysis. Telemedicine intervention had a significant effect on the change of systolic (MD -6.05; 95% CI -6.23, -5.87; $p < 0.00001$; I^2=84%) and diastolic (MD -2.76; 95% CI -4.13, -1.39; $p < 0.0001$; I^2=89%) blood pressure control. Telemedicine intervention was also associated with lower stroke recurrence (OR 0.82; 95% CI 0.42, 1.59; p=0.55; I^2= 70%) and mortality rate (OR 0.87; 95% CI 0.68, 1.12; p=0.28; I^2=0%). Therefore, telemedicine applications may be a promising strategy to optimize the implementation of stroke secondary prevention. More up-to-date trials with higher quality are needed to confirm our findings and assess the other outcomes of telemedicine intervention, such as cost-effectiveness, medical adherence, and quality of life outcomes.

Keywords : stroke ; secondary prevention ; telemedicine ; blood pressure ; mortality

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Introduction

Stroke is a neurological deficit that occurs suddenly due to the disruption of blood flow in the central nervous system, including cerebral infarction, subarachnoid hemorrhage (SAH), and intracerebral hemorrhage (ICH) [1]. According to data from 2019, stroke is the second most common cause of death, accounting for 11.6% of deaths worldwide [2]. It is also the biggest reason for severe long-term disabilities that restrict stroke survivors' mobility. Thus, stroke has become an economic burden due to therapy and post-stroke care both in developed and developing countries [3].

Patients with a history of stroke have a higher susceptibility to recurrent stroke. The prevalence of recurrent stroke occurs in 25-30% of patients referred for stroke in the hospital, and usually, stroke recurrence causes more severe disability and poorer prognosis [4]. Therefore, improving stroke secondary prevention to reduce the risk of recurrent strokes in people who have already had a stroke is required. Several strategies that are effective in preventing recurrent stroke include control of blood pressure, lowering cholesterol, and antithrombotic therapy [5-7]. However, long-term management of stroke risk factors to prevent recurrent stroke has not been optimal in its implementation [8].

Telemedicine is a form of remote delivery of healthcare services, including examinations, consultations, and monitoring via telecommunications and computer technologies. Telemedicine allows health care providers to deliver healthcare services and health education without needing an in-person visit [9]. The COVID-19 pandemic has affected the health services system for stroke [10]. The use of telemedicine is increasing and is a solution for post-stroke patients whose regular medical follow-up has been limited due to the COVID-19 pandemic. Telemedicine is becoming an increasingly common way to optimize the implementation of improving therapy compliance, lifestyle modification, and long-term risk factors control, such as blood pressure monitoring, and it is expected to reduce stroke recurrence events and mortality [11].

More outcomes such as systolic along with diastolic blood pressure, stroke recurrence, and mortality after telemedicine intervention as stroke secondary prevention have yet to be comprehensively reviewed. In addition, telemedicine has been rapidly growing recently, so that updated review is needed. Therefore, we want to create an evidence base for the effectiveness of telemedicine as secondary prevention among stroke survivors. This study is a systematic review and meta-analysis of randomized controlled trials (RCTs) that aim to evaluate the evidence of telemedicine's effects on systolic blood pressure, diastolic blood pressure, stroke recurrence, and mortality in post-stroke patients.

Methods

Search Strategy

This paper follows the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. A systematic search was conducted through PubMed, Science Direct, Scopus, Web of Science, and ProQuest databases, searching for studies from 2018 to 2022. The following search query ("Stroke" OR "Strokes" OR "Brain Infarction" OR "Transient Ischemic Attack" OR "Ischemic Stroke" OR "Hemorrhagic Stroke" OR "Embolic Stroke" OR "Thrombotic Stroke") AND ("Telemedicine" OR "Telemonitoring" OR "Telestroke" OR "Digital Health Technology" OR "Telehealth" OR "E-health" OR "Mobile Health") was used. Only papers written in English, a language that the authors could comprehend, were allowed to be included in this review.

Eligibility Criteria

Inclusion criteria to filter the result were set as: (1) study design as randomized controlled trials (2) subjects as post-stroke patients of all types (ischemic stroke/hemorrhagic stroke/embolic stroke/thrombotic stroke) or post-transient ischemic attack patients (3) intervention as telemedicine for stroke. Exclusion criteria were also applied: (1) irretrievable full text articles and (2) language other than English.

Quality assessment

To assess the quality of the included studies, Instrument of Cochrane Risk of Bias Tool 2 (ROB 2) for randomized controlled trials was used. The ROB 2 tool consists of three judgments: low risk of bias, some concerns, or high risk of bias. There were 5 domains that were assessed. Reviewers evaluated the possibility of bias in studies cooperatively through group discussion.

Data Extraction and Statistical Analysis

Study information (author, year, country), intervention characteristic, duration of the study, subject characteristic (including sample size, sex, age of participants), stroke recurrence, mortality, systolic and diastolic blood pressure after the intervention compared to the baseline were all extracted. All reviewers worked independently to extract data by filling out an extraction data table. If any conflicts were found, discussion with the other reviewers were conducted.

Review Manager 5.4 for Windows was used to perform the statistical analysis. This review pooled continuous data in mean difference (MD) ±SD with 95% CI, while the dichotomous outcome was summarized using odd ratio (OR) with 95% CI. P value of less than 0.05 is considered significant statistically. To measure heterogeneity, the I^2 was utilized. Low heterogeneity was defined as 0-50 percent, moderate heterogeneity as 50 percent–75 percent, and high heterogeneity as $I^2 > 75$ percent. The random-effects model was chosen if there was high heterogeneity throughout the studies, and the fixed effects model was used if there was low heterogeneity. The forest plot was used to visually illustrate the effect of the intervention.

Results

Study Selection

Search results of published studies from PubMed, Science Direct, Scopus, Web of Science and ProQuest database from 2018 to 2022 were a total of 889 articles. The authors used an automation tool to remove a total of 241 duplicate articles. Then, the authors assess the titles and abstract of 648 articles. About 524 articles were excluded due to irrelevant title and abstract. Full-text was retrieved from 124. However, 2 articles were wrong in publication-type and 1 article was written in foreign language. Then, the authors assess the report for eligibility, 63 articles were wrong study design, 3 articles had the wrong population, 19 articles had the wrong outcome, and 28 articles were not RCT. The final study selection resulted in 6 articles included in our study. Further details on the literature search strategy are displayed on figure 1.

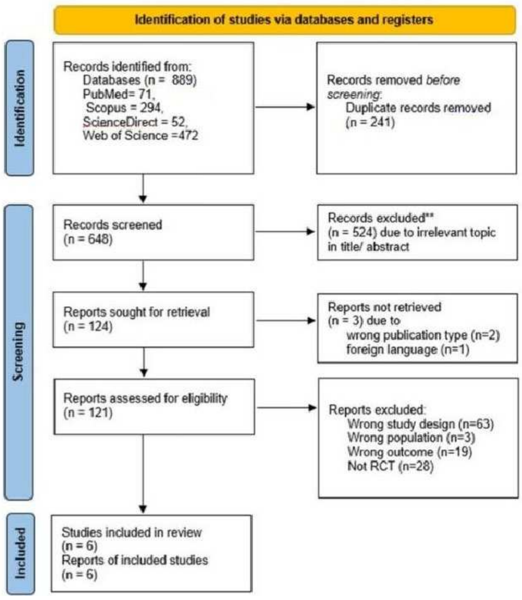

Figure 1. PRISMA flowchart in the systematic search

Study Characteristics and Quality Assessment

The study characteristics are displayed in figure 2. Two studies were conducted in Europe (Germany, Denmark, and Sweden), three studies were conducted in Asia (Korea, Ghana, and China), and one study was conducted in America (US). The included studies ranged in duration from three months to three years. Post strokes patients participated as the study's subjects. The individuals' mean ages ranged from 55 to 69.9 years. Males composed between 57.3 and 76.9 percent of the population. The quality of the studies were comprehensively evaluated using Risk of Bias 2 (RoB 2) tools. The quality assessment in three studies revealed low risk and three studies classified as some concerns. There were no studies considered as high-risk bias. The risks of bias were summarized on figure 3.

Author, Year	Country	Intervention	Duration	Total Sample	Male (%)	Age	SBP	DBP	Stroke Recurrence	Mortality
							Intervention vs Control			
Ahmadi, 2019	German and Denmark	Telehealth multifactorial support programme	2 years	908 vs 905	65.7% vs 66.7%	67.1 ± 10.4 vs 67.7 ± 10.4	130.1 ± 16.3 vs 135.4 ± 18.2	80.4 ± 10.6 vs 80.0 ± 9.6	122/1030 vs 119/1042	73/1030 vs 75/1042
Kim, 2020	Korea	Intensive telehealth monitoring	1 year	31 vs 29	61% vs 69%	60 ± 12 vs 56 ± 10	n/a	n/a	2/31 vs 1/29	0/31 vs 0/29
Lakshminarayan, 2018	US	mHealth based hypertension management	3 months	26 vs 24	76.9% vs 68%	63.1± n/a vs 68.3± n/a	130.2 ± 11.4 vs 139.8 ± 16.3	n/a	n/a	n/a
Ogren, 2018	Sweden	Telephone-based counselling	3 years	320 vs 340	59.4% vs 59.1%	69.9± n/a vs 69.3± n/a	128.1 ± 1.2 vs 134.2 ± 1.2	75.3 ± 0.8 vs 78.8 ± 0.8	n/a	44/320 vs 55/340
Sarfo, 2019	Ghana	Blue-toothed BP device and a monitoring app	9 months	30 vs 30	60% vs 70%	55 ± 13 vs 55 ± 13	n/a	n/a	28/30 vs 27/30	1/30 vs 1/30
Yan, 2021	China	A primary care-based integrated mHealth	12 months	637 vs 662	57.3% vs 57.6%	65.7± 8.2 vs 55 ± 13	138.9 ± 20.9 vs 141.4 ± 23.7	74.1±11.6 vs 77.4±11.7	27/611 vs 57/615	11/611 vs 19/615

Figure 2. Study characteristic

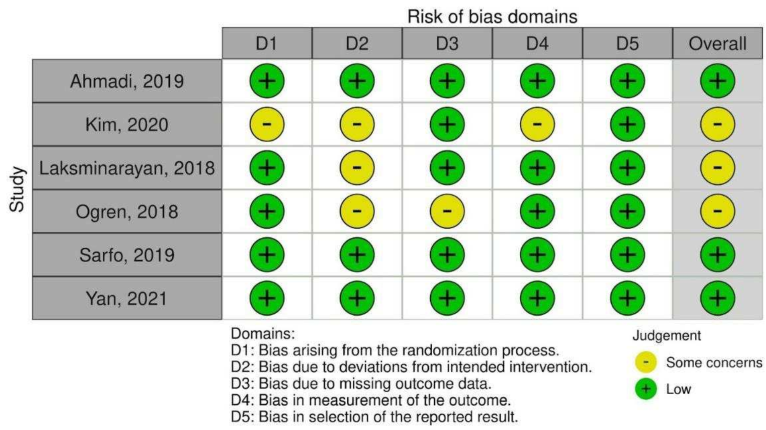

Figure 3. The Risk of Bias Assessment

Systolic Blood Pressure

Changes in systolic blood pressure from the baseline until after receiving telemedicine intervention were pooled on a total of 3822 patients (experimental n=1891, control = 1931). The meta-analysis revealed that the telemedical intervention had a statistically significant impact on systolic blood pressure control (MD -6.05; 95% CI -6.23, -5.87; $p < 0.00001$; I^2=84%). There was high heterogeneity between studies (I^2=84%) (Figure 4).

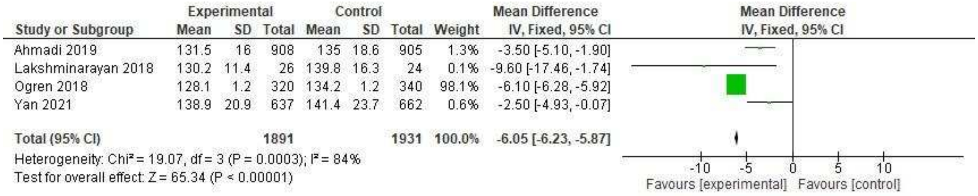

Figure 4. Forrest plot analysis of systolic blood pressure

Diastolic Blood Pressure

Changes in diastolic blood pressure from the baseline until after receiving telemedicine intervention were pooled on a total of 3772 patients (experimental n=1865, control = 1907) for diastolic blood pressure data. The meta-analysis revealed that the telemedical intervention had a statistically significant impact on diastolic blood pressure management (MD -2.76; 95% CI -4.13, -1.39; $p < 0.0001$; I^2=89%). There was high heterogeneity between studies (I^2=89%) (Figure 5).

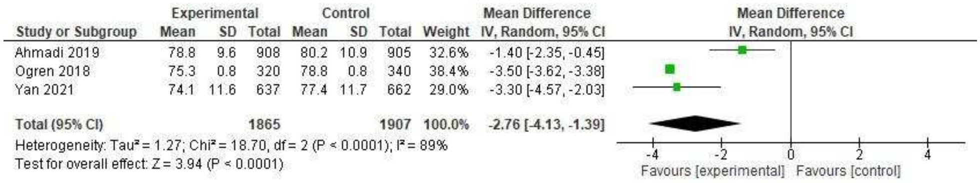

Figure 5. Forrest plot analysis of diastolic blood pressure

Stroke Recurrence

Stroke recurrence data were pooled on a total of 3418 patients (experimental n = 1702, control = 1716). In terms of stroke recurrence, the experimental and control groups did not differ significantly from one another. However, the telemedicine intervention group had a lower risk of recurrent stroke (OR 0.82; 95% CI 0.42, 1.59; p=0.55; I^2= 70%). Stroke recurrence outcomes showed moderate heterogeneity (I^2 = 70%) (Figure 6).

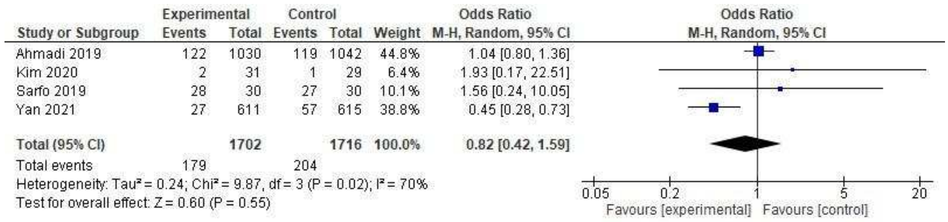

Figure 6. Forrest plot analysis of stroke recurremce

Mortality

Mortality data were pooled on 4078 patients (experimental n=2022, control=2056). The experimental and control groups did not differ significantly from one another, however the telemedicine intervention group had a lower rate of mortality (OR 0.87; 95% CI 0.68, 1.12; p=0.28; I^2=0%). Mortality outcomes showed no heterogeneity (I^2 = 0%) (Figure 7).

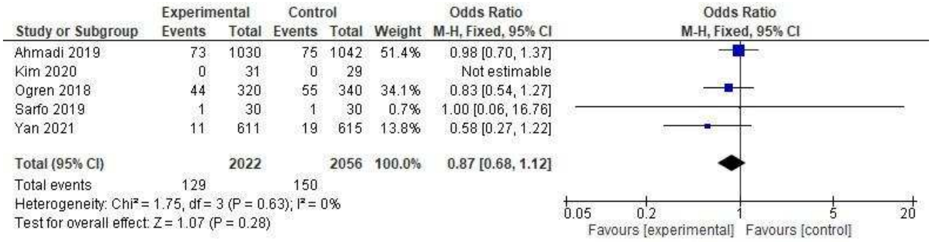

Figure 7. Forrest plot analysis of mortality

Discussion

Stroke has a high mortality and recurrence rate, hence managing and reducing stroke risk factors is necessary for secondary prevention [2,4]. This study's objective was to evaluate the evidence of telemedicine effects on systolic along with diastolic blood pressure, stroke recurrence, and mortality in post-stroke patients as a secondary prevention strategy. This study calculates meta-analysis for systolic along with diastolic blood pressure, stroke recurrence, and mortality from two groups: stroke survivors that received telemedicine intervention as the experimental group and stroke survivors that received usual care as the control group. This study included six randomized controlled trials with 3942 participants.

We chose blood pressure as the outcome of secondary prevention because studies found a significant effect of blood pressure control on the incidence of recurrent stroke [12]. In terms of lower values in the experimental group, the meta-analysis demonstrated a statistically significant effect of the telemedical intervention on both systolic blood pressure control (MD -6.05; 95% CI -6.23, -5.87; $p < 0.00001$; I^2=84%) and diastolic blood pressure control (MD -2.76; 95% CI -4.13, -1.39; $p < 0.0001$; I^2=89%). It indicates that when compared to standard care, the average decrease in systolic and diastolic blood pressure following telemedicine intervention was -6.05 mmHg and -2.76 mmHg, respectively. Because studies have shown that maintaining normal blood pressure with a 3 mmHg reduction in systolic blood pressure is estimated to reduce stroke mortality by 10% and ischemic heart disease and other vascular diseases by 8%, this finding emphasizes the benefits of telemedicine as secondary prevention of stroke in the population [13]. In addition, studies suggest a reduction in stroke recurrence risk of approximately 40% if the patient can control blood pressure within the recommended range (<140/85 mmHg or 130/80 mmHg for diabetic patients) [14]. Thus, controlling blood pressure to achieve the target is essential in secondary stroke prevention efforts.

The meta-analysis reported a non-significant difference between the control and intervention groups in terms of stroke recurrence (OR 0.82; 95% CI 0.42, 1.59; p=0.55; I^2= 70%). This insignificant result could be due to the high number of patients in the control group who had already met the secondary prevention target so that it could dilute the outcome of the telemedicine intervention effect [15]. Thus, further studies are expected to narrow the subject to patients who have not met the recommended secondary prevention targets, for example, stroke patients who have just been discharged from the hospital. The difference of the mortality data did not possess statistically significant value (OR 0.87; 95% CI 0.68, 1.12; p=0.28; I^2=0%). Even though there were no significant differences in the outcomes of stroke mortality and recurrence between the control and intervention groups, the telemedicine intervention group had a reduced rate of stroke recurrence and mortality than the usual care group. Thus, the optimal use of telemedicine can be a strategy that can contribute to stroke secondary prevention. The lower rate of recurrence of stroke and mortality in this study is in line with a study conducted by Pietrzak that internet-based interventions provide promising outcomes in cardiovascular disease [16]. Ferrante also found the same thing, a reduction in mortality and hospitalization rates can be achieved with telephone-based interventions in chronic heart failure patients [17].

Included studies in this paper consist of various types of telemedicine used. The study conducted by Ahmadi and Ogren was telephone-based, the study conducted by Lakshminarayan, Yan, and Sarfo used an integrated health application on the smartphone, while the study conducted by Kim used a combination of telephone, application, and messaging services [11,15,18-21]. Studies have shown that poor self-management of stroke risk factors, low stroke knowledge, and poor adherence to medication are the potential causes of recurrent stroke [22]. The better outcome of the telemedicine intervention group is probably due to the fact that telemedicine can improve stroke risk factors management and drug compliance. Telemedicine makes it easier for patients to communicate with healthcare workers if needed so that healthcare workers know the patients' crucial parameters to cure the disease [11,15,18-21]. Better blood pressure control can be achieved by seeking more tight control of blood pressure, especially for patients with hypertension [19]. Telemedicine intervention may be a promising approach to increase the frequency of blood pressure measurements. This is because, with telemedicine, we can collect, send, and record blood pressure data without the need for an in-person visit so that patients can monitor their blood pressure more often and more easily to do daily self-monitoring. The data about the patient's blood pressure on a regular basis allow health workers to evaluate the patient's condition more often and can make it easier to adjust the medication needed by the patient at that time [11,19,21].

Health education efforts can also be maximized with telemedicine, considering that nowadays the wider community can already reach mobile technology [9]. The education carried out is to provide comprehensive information regularly about the pathophysiology and a person's risk for recurrent stroke. Education can also be in the form of the importance of controlling blood pressure and the strategies that need to be done to prevent recurrent strokes, such as lifestyle modification, doing physical activities, and increasing medical adherence with automated reminders that are not available in usual care [15,19-21]. Patients can also periodically be given feedback and motivation through telemedicine [15].

Given that trials included in this paper involve many different countries, the review's findings demonstrate that telemedicine can be applied to patients from various health systems and countries (Germany, Denmark, Korea, The United States, Sweden, Ghana, China). This review has some limitations, including the inclusion of just English-language studies, which may have led to the exclusion of additional relevant studies. In addition, although this study did not find high-risk bias, there were three studies that yielded some concern bias. Further studies are expected to have better quality to confirm the results of this review. More recent, higher-quality trials are required to investigate the other effects of telemedicine intervention, such as cost-effectiveness, medical adherence, and quality of life outcomes.

Conclusion

According to this study, there was a significant decrease in blood pressure control between the experimental and control group. The average systolic and diastolic blood pressure reduction following telemedicine intervention was -6.05 mmHg and -2.76 mmHg, respectively. Telemedicine intervention was also associated with lower stroke recurrence and mortality than usual care. Therefore, telemedicine applications may be a promising strategy to optimize the implementation of stroke secondary prevention. More recent, higher-quality trials are required to confirm our findings and evaluate the other effects of telemedicine intervention, such as cost-effectiveness, medical adherence, and quality of life outcomes.

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