Original Article

Smartphone-Based Telestroke Vs"Stroke Physician" led Acute Stroke Management (SMART INDIA): A Protocol for a Cluster-Randomized Trial

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Abstract

Background: One of the major challenges is to deliver adequate health care in rural India, where more than two-thirds of India's population lives. There is a severe shortage of specialists in rural areas with one of the world's lowest physician/population ratios. There is only one neurologist per 1.25 million population. Stroke rehabilitation is virtually nonexistent in most district hospitals. Two innovative solutions include training physicians in district hospitals to diagnose and manage acute stroke ('Stroke physician model') and using a low-cost Telestroke model. We will be assessing the efficacy of these models through a cluster-randomized trial with a standard of care database maintained simultaneously in tertiary nodal centers with neurologists. **Methods:** SMART INDIA is a multicenter, open-label cluster-randomized trial with the hospital as a unit of randomization. The study will include district hospitals from the different states of India. We plan to enroll 22 district hospitals where a general physician manages the emergency without the services of a neurologist. These units (hospitals) will be randomized into either of two interventions using computer-generated random sequences with allocation concealment. Blinding of patients and clinicians will not be possible. The outcome assessment will be conducted by the blinded central adjudication team. The study includes 12 expert centers involved in the Telestroke arm by providing neurologists and telerehabilitation round the clock for attending calls. These centers will also be the training hub for "stroke physicians" where they will be given intensive short-term training for the management of acute stroke. There will be a preintervention data collection (1 month), followed by the intervention model implementation (3 months). **Outcomes:** The primary outcome will be the composite score (percentage) of performance of acute stroke care bundle assessed at 1 and 3 months after the intervention. The highest score (100%) will be achieved if all the eligible patients receive the standard stroke care bundle. The study will have an open-label extension for 3 more months. **Conclusion:** SMART INDIA assesses whether the low-cost Telestroke model is superior to the stroke physician model in achieving acute stroke care delivery. The results of this study can be utilized in national programs for stroke and can be a role model for stroke care delivery in low- and middle-Income countries. (CTRI/2021/11/038196)

Keywords: Cluster randomized trial, stroke, telestroke, telerehabilitation

Introduction

With more than 1.2 billion population and 18% of the world population living in India, we are nations within a nation with an ongoing epidemiological transition with an enormous increase in noncommunicable diseases.[1] Stroke is a leading cause of mortality in India, with more than 1.5 million cases every year. One of the major challenges is to deliver adequate health care in rural India, where more than two-thirds of population lives, whereas 75% of India's health resources are concentrated in urban cities.[2] There is a severe shortage of specialists in rural areas with one of the lowest physician/population ratios in the world (0.6 per 1000 people). There is only one neurologist per 1.25 million population. Moreover, there is hardly any availability of stroke rehabilitation services in district hospitals.

Two innovative solutions include training physicians in district hospitals to diagnose and manage acute stroke ('Stroke physician model') or using technology to bridge the distance between a neurologist and patient via a low-cost Telestroke model.[3] India is undergoing a revolution in mobile phone technology where most mobile companies are giving 1–1.5 GB of data free per day

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to their customers. In a resource-limited setting like India, the most advanced telemedicine models may not be cost-effective and cannot penetrate semi-urban or rural areas.[4,5]

On the other hand, the training of general physicians in district hospitals may obviate the need for a neurologist in acute stroke management. Every district hospital in India has at least one general (i.e., internal medicine) physician. Hence, this alternative low-cost model for stroke care is to create a cadre of "stroke physicians" and make the district hospitals stroke-ready. "Stroke Physicians" which we intend to train are different from the vascular neurologists of developed countries. These are general physicians who are given intensive short-term training in acute stroke management. Similar approaches are being tried in China.[6] But whether this short-term training given to physicians will lead to sustained results in acute stroke care is unknown, especially when this same physician has to manage snake bites, organophosphorus poisoning, malaria, myocardial infarction, and other numerous emergencies in the district hospital.

We hypothesize that the "low-cost Telestroke model" is superior to the "stroke physician model" to deliver optimal acute stroke care delivery. We plan to conduct a multicenter cluster-randomized trial in 22 district hospitals and 12 nodal centers.

Methods

Study design: SMART INDIA trial is an academic investigator-initiated, open-label, multi-center cluster-randomized trial assessing the efficacy of two-stroke care delivery models (Stroke physician model and Low-cost Telestroke model). The study has been approved by the ethics committee of all nodal centers. Informed consent will be taken from each patient included in this trial and/or their relatives.

Setting: The study plans to recruit 12 nodal centers and 22 district hospitals from various states in India. The nodal centers will be tertiary centers where neurologists manage acute stroke care. At present, we have recruited seven nodal centers and 15 district hospitals.

Inclusion criteria for a unit of a cluster (district hospital)

1. District hospitals where only physicians are available.
2. Physicians willing to use a smartphone with 24/7 internet access.
3. Availability of CT scan.

Exclusion criteria for a unit of a cluster (district hospital)

1. Availability of a neurologist in the hospital.
2. Lack of smartphone or internet access.

Inclusion criteria for patient recruitment inside a cluster unit

1. Adults with acute stroke (up to 1 week).
2. Informed consent to participate in the study.

Randomization, Allocation, and Blinding

Twenty-two units (district hospitals) satisfying the eligibility criteria and recommended by the 12 nodal centers will be recruited. The participating hospitals' administration should allow the hospital to be allocated to one of the two interventions (Telestroke or 'stroke physician model'). These units (hospitals) will be randomized into either of two interventions using computer-generated random sequences with allocation concealment. Blinding of patients and clinicians is not possible, but a blinded central outcome adjudication team will do the primary outcome assessment.

Study workflow

1. Development and pilot testing of low-cost Telestroke model.
2. Training workshop for all physicians in district hospitals.
3. Baseline data collection (district hospitals and nodal centers) – Month Zero.
4. Intervention
5. Outcome assessment at 1 and 3 months.
6. Open-label extension of low-cost Telestroke model for all district hospitals.

***Development of pilot testing of low-cost Telestroke*:** We developed the "SMART-India App," a phone application with the primary purpose of providing low-cost Telestroke services of a neurologist and physiotherapist to physicians in district hospitals. A pilot testing was conducted in all the nodal centers. A summary of the workflow of the App is described in Figure 1.

The Smart India app was designed and developed over 8 months (December 2020–July 2021). The android version of the SMART-INDIA Stroke-App is available in the play store, where access is restricted to study participants [physicians, neurologists, physiotherapists, and data entry operators (DEO)]

Neurologists, physicians, physiotherapists, research coordinators, DEOs from recruited nodal centers and district hospitals are registered with their name, email, and mobile number in the App through the Smart India website. All nodal centers are interconnected with their respective district hospitals. Whenever a patient with acute stroke reaches activated centers, a physician at the district hospital will log in SMART INDIA APP immediately and start entering the detail of the stroke patient. Neurologists will receive a notification alert in the App on their phone immediately. The neurologist and physician interact in the chat box and decide on specific management. After planning on acute stroke management, the neurologist will end the chat, and a call request for telerehabilitation to a study/notified physiotherapist will be activated.

Telerehabilitation

The Telerehabilitation component of SMART-INDIA was developed to provide knowledge and guidance about poststroke rehabilitation to the physicians managing stroke patients. As physiotherapy is an integral part of stroke management apart from preventive and thrombolytic interventions, the telerehabilitation component of the "Smart India App" consists of detailed neuro-physiotherapy assessment followed by

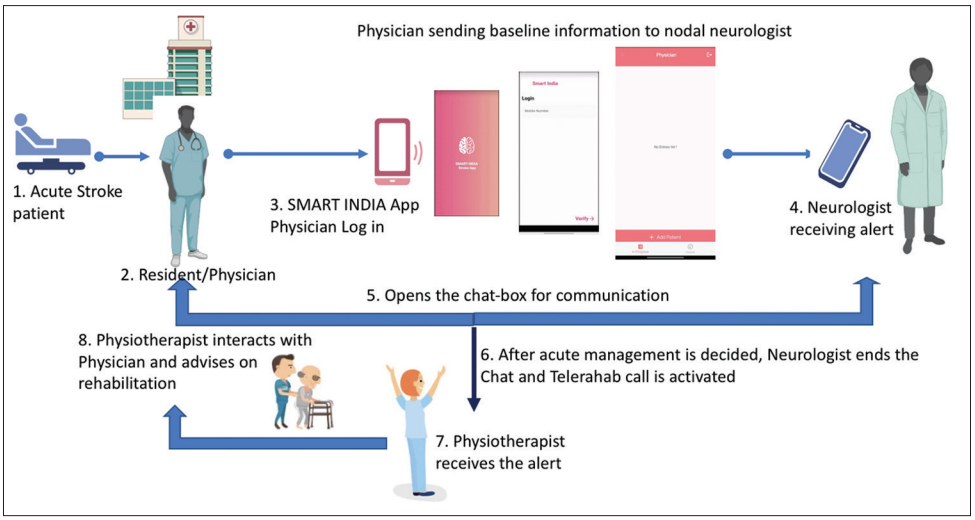

Figure 1: SMART INDIA Work flow

treatment goals. The management plan includes images and pre-recorded videos with volunteers and therapists explaining various rehabilitative interventions for the face, upper, and lower limbs. Once the notification for telerehabilitation is received, the chat window opens between the physiotherapist at All India Institute of Medical Sciences (AIIMS) and the district physician. The physiotherapist interacts with the physician and advises on physiotherapy tailored for the enrolled patient through videos and images mentioned in the App. The dialogue box closes, and the case is closed once the neurorehabilitation management is achieved with a home exercise plan at discharge.

Training workshop: We conducted an online workshop involving neurologists from the tertiary nodal centers and physicians in district hospitals. The workshop included interactive sessions on diagnosis and management of acute stroke, neuroimaging, nursing care, and essential stroke rehabilitation. Feedback was taken from nodal centers and physicians in district hospitals, and further sessions were planned over the next 1 month. All physicians will have to be certified in National Institutes of Health Stroke Scale (NIHSS) and modified Rankin scale assessment.

Baseline data collection (month zero): A data entry operator from the nodal center will collect the data using the SMART-INDIA App from the nodal center and district hospital. The first 1 month of the study will be the collection of the baseline (preintervention) data, giving an idea of the existing stroke care services. During this period, the physicians randomized to the Telestroke arm will be trained to use the App.

Intervention: Two stroke care intervention models will be assessed in this study.

a. Low-cost Telestroke model: The physicians of the district hospitals who get randomized to this arm will use the SMART-INDIA App to contact the neurologists in the designated nodal center to manage any acute stroke patients, including both the hyperacute stroke management in the window period as well as in-hospital stroke care. The expert neurologist will be available 24 × 7 to discuss any issues related to acute stroke patients till the time of discharge. The physicians will also have access to
b. "Stroke Physician model": The initial common training on stroke management will be given to all physicians in both arms. The physicians in the "Stroke Physician model" will continue to manage acute stroke patients as part of their normal working pattern enhanced by their training in the workshops.

Outcomes

The primary outcome will be the composite score (percentage) of performance of acute stroke care bundle at 1 month and 3 months [Figure 2]. The highest score (100%) will be achieved if all the eligible patients receive the standard stroke care bundle. The central outcome adjudication team will determine the primary outcome after analyzing anonymized blinded data for each patient recruited. The primary outcome will be assessed at 1 month and 3 months which will be the two coprimary outcomes.

We selected 24 quality of care bundles based on measurability, underlying evidence, clinical importance, and likely noncompliance encountered in district hospitals. Data will be extracted from the patient medical records by independent research staff from the expert center assigned to that district hospital. The outcome bundles will also be collected in the expert centers simultaneously as the preintervention period of clusters.

Components of the Stroke care bundle are

Acute stroke care bundle

1. Thrombolytic agent door-to-drug <60 min [acute ischemic stroke (AIS)].
2. Symptom onset to thrombolytic agent <180 min (AIS).
3. A thrombolytic agent is given only to those without contraindications (AIS).

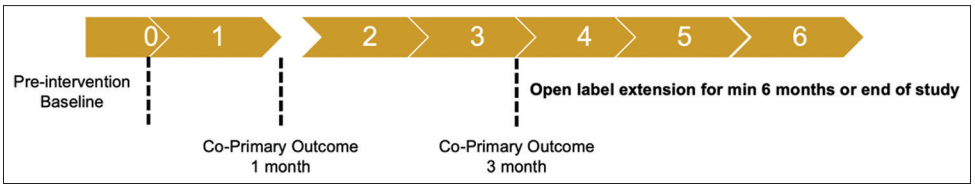

Figure 2: Time line of Outcome assessment

NIHSS was performed for acute ischemic stroke (AIS).

4. Discussing option for referring a patient with large vessel occlusion (LVO) for mechanical thrombectomy (MT) to a referral center (AIS).
5. Antihypertensive medications initiated to reduce BP or assessed for their indication for use (Intracerebral hemorrhage (ICH)/AIS).
6. Glasgow Coma Scale (GCS) monitoring.
7. ICH score calculated (ICH).
8. Surgical options were discussed with patients.

In-hospital care bundle

1. Aspirin administered within 48 h (AIS).
2. Smoking cessation counselling.
3. Early mobilization within 48 h.
4. Dysphagia screening test.
5. Evaluation for Atrial fibrillation- Holter (AIS).
6. Venous thromboembolism prophylaxis.
7. Evaluated for physiotherapy within 48 h.

Discharge bundle

1. Treatment of hypertension in newly diagnosed patients or continuing hypertensive drugs for previously known hypertensive patients.
2. Anticoagulants in atrial fibrillation (AF) patients (AIS).
3. Antithrombotic drugs in those patients without AF (AIS).
4. Discharged on statin medication (AIS).
5. Rehabilitation package and measures of improvement on ADL.

Follow up bundle

1. Modified Rankin Score at 90 days.
2. Received rehabilitation.
3. Risk factor control monitoring (Blood pressure, Blood sugar, international normalized ratio (INR) for those on anticoagulation) .

Examples of outcome assessment

Case: A 75-year-old lady with a history of hypertension presented with acute right hemiparesis to a district hospital. She reached the hospital after 2 h of the onset of stroke. The patient underwent a CT scan and was thrombolyzed. NIHSS was not done, and the option of LVO was not considered (CT angiography was not done). The patient was not given the option of referral to a tertiary center. In the hospital, she was managed with Aspirin 150 mg. The patient did not undergo a dysphagia screening test, smoking cessation counseling, early mobilization, evaluation for AF, venous thromboembolism prophylaxis, or physiotherapy evaluation. At discharge, her hypertensive drugs were continued along with aspirin and statin. No stroke rehabilitation measures were advised. During follow-up, ºModified Rankin Scaleº(mRS) was not documented, and the patient did not receive any rehabilitation. Blood pressure and blood sugars were monitored.

Primary outcome assessment: In this patient with acute ischemic stroke, the blinded central data adjudication team will assess what percentage of the eligible components of the stroke care bundle was fulfilled by the physician. The eligible components of the stroke care bundle, in this case, are points 3–6 of acute care bundle, 1–7 of in-hospital care bundle, 1, 3–5 of discharge bundle, 1–3 of follow up bundle. Out of a total of 19 eligible care bundles, the physician was able to deliver 7 components (7/19 = 36.8%)

Secondary outcomes

- The proportion of patients achieving mRS 0–2 at 3 months.
- The proportion of patients who received aspirin within 48 h.
- The proportion of patients who received smoking cessation.
- The proportion of patients who received dysphagia screening.
- The proportion of patients who received venous thromboembolism prophylaxis.
- The proportion of patients who were evaluated for physiotherapy.
- The proportion of patients with newly diagnosed atrial fibrillation.
- The proportion of patients with AF who received anticoagulation.
- The proportion of patients without AF who received antiplatelets.
- The proportion of patients who received statins.
- The proportion of patients who received rehabilitation.

We will also compare composite scores between Telestroke model and Standard of care (Nodal centers), the composite score between Stroke physician model Vs Standard of care (Nodal centers), and secular trend in each of the care bundles (acute stroke, in-hospital, discharge summary, and follow up) pre- and postintervention.

Data safety and monitoring board (DSMB)

The study will be conducted according to Good Clinical Practice (GCP) guidelines. A data safety and monitoring board will independently review the efficacy and safety data

of the study. The DSMB is composed of an independent stroke neurologist, general physician, and statistician. No formal interim analyses for efficacy or futility are planned.

Sample size and Statistical Analysis

The study will use a cluster randomized controlled trial design with pre test and post-test repeated cross-sectional measures. The primary analysis will be an intention to treat. The 24 measures are grouped into four bundles (acute management, in-hospital management, discharge advice, and follow-up). The pre- and postintervention performance will be assessed for each bundle and each outcome measure.

The sample size was calculated for the primary outcome (composite score (percentage) of performance of stroke care bundle) based on a cluster-randomized trial conducted to improve stroke care in Minnesota.[7] They had considered a baseline performance of 50% and a performance difference of 5%–7%. When we assume a baseline performance of 50%, a performance difference of 5% between two interventions with intracluster correlation coefficient (ICC) of 0.005, size of each cluster 50, 80% power, and 5% α error, the number of clusters required are 22 with a required sample size of 166 per cluster and a total sample size of 3652 patients. From our experience in the Telestroke study in Himachal Pradesh, we know that the baseline performance will be around 20% in district hospitals without neurologists. Hence, a baseline performance of 20% with all other similar parameters yielded 36 clusters and an 1819 sample size. We have taken the more conservative and feasible cluster size (22) and total sample size (3652).

Quantitative variables will be summarized using mean (SD) or median (Q1, Q3) as suitable upon checking for normal distribution. Categorical variables will be summarized as frequency and proportions. Baseline characteristics will be compared across the two interventions (Telestroke or "stroke physician model") using independent samples t-test or Fisher's exact test as applicable. The primary analysis for each outcome, specifically the outcome [composite score (percentage) of performance of stroke care bundle], will be intention-to-treat (ITT) analysis viz, participants with their outcome recorded will be analyzed according to the group to which they are allocated initially and regardless of whether or not the treatment and follow-up schedule was adhered to. A per-protocol (PP) analysis will also be carried out. The analysis will be based on the individual-level data allowing for the clustering between individuals within the same hospital [as the trial includes a reasonable number of clusters (22 hospitals)]. A covariate-adjusted analysis will be performed as applicable. An intraclass correlation coefficient along with a 95% confidence interval (CI) will be reported for outcome based on the adjusted analysis. Unadjusted between-group differences will also be presented for comparison between adjusted and unadjusted analyses performed. All the outcomes will be compared between the groups using unpaired t-test/Wilcoxon rank-sum test and within the group (from baseline to 1 month; from baseline to 3 months) using paired t-test/Wilcoxon signed-rank test/repeated measures analysis of variance (ANOVA) as suitable. Adopting a similar approach, data in the two interventions (Telestroke or "stroke physician model") will also be compared with the standard of care. The results will be presented as difference and 95% CI. The statistical tests used and the CIs presented will be two-sided. The significance level is fixed at 5% and will be consistent throughout. The statistical analysis will be done using Stata v. 16 (College Station, Texas, USA).

Study organization and funding

The study is funded by the Department of Health Research, Indian Council of Medical Research (DHR-ICMR), Government of India.

Discussion

India is home to one of the lowest physician/population ratios globally despite bearing a significant share of the global burden of stroke. The situation is worsened by the presence of only one neurologist per 1.25 million population. Real-time interaction between the physician, neurologist, and physiotherapist via a low-cost solution is a need of the hour.

SMART INDIA trial, an academic investigator-initiated, open-label, multi-center cluster-randomized trial, strives to compare a Stroke physician model with a Low-cost Telestroke model (based on a smart phone app) at 12 nodal centers and 22 district hospitals from various states in India.

The tele-stroke arm harnessing the power of information technology via a smartphone app enables the physician at the district hospital to engage in a real-time consultation with a stroke neurologist. The App allows the physician to transmit valuable patient data, including CT scans, critical for making timely clinical decisions in patient management. Following acute stroke care, the App facilitates interaction between the caregiving physician and a physiotherapist skilled in stroke rehabilitation via a tele-rehab module. The tele-rehab module incorporated in the App provides physiotherapy management and home rehabilitation curated specifically to the patient and type of stroke. This App will offer a viable avenue to meet the rehabilitation needs of stroke survivors in resource-limited rural settings in low- and middle-income countries like India, where stroke burden is rapidly escalating.

Conclusion

A daunting asymmetrical burden on health care, involving stroke and neurologists, requires out-of-the-box solutions. The combination of omnipresent internet connectivity beyond the confines of cities and ready availability of smartphones at the hands of every physician has the potential to fill the painful void that separates the helpless neurologist from "Health care for all." A low-cost smartphone app may be the solution India had been waiting for. The planned cluster **randomized**

controlled trial (RCT) will assess the superiority hypothesis of SMART-INDIA App over "Stroke Physician model."

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Ethical approval

Taken from all centres.

Declaration of Conflicts of Interest

All the authors declared that they have no conflicts of interest regarding authorship, research or publication of this article.

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Conflicts of interest

There are no conflicts of interest.

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