Optimizing the use of digital sensors (non-invasive) for early detection of risk factors for recurrent stroke to improve quality of care: A systematic review [version 1; referees: awaiting peer review]

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Abstract

**Background:** Improving awareness in patients with stroke to detect risk factors of recurrent stroke has recently become a major challenge for all health professionals in preventing recurrence among stroke survivors. Utilization of advanced technology, such as digital sensors, (a non-invasive device) is among the breakthroughs in detecting the risk of disease and promotes more effective prevention and improves quality of care. This study aims to conduct a systematic review on studies addressing early detection of the risk factors of recurrent stroke through the utilization of digital sensors.

**Methods:** A literature search was carried out on articles published between 2011 - 2018 on EBSCO, Elsevier, Science Direct, ProQuest, Springer link, PubMed, MEDLINE, PLoS, and the Journal of Community Nursing. The search identified quantitative research studies on the utilization of digital sensors in cases of hypertension, diabetes mellitus, hypercholesterolemia, and cardiac disorders that contributed to stroke recurrence. Each study's bias was assessed using Review Manager 5.

**Results:**
Ten articles were analyzed through data extraction. Robust assessment of independent risk factors which provoke recurrent stroke such as hypertension, diabetes mellitus, hypercholesterolemia, and heart diseases could lead to conservation of health resources. It is very important to monitor these factors. With the development of technology, the potential use of non-invasive monitoring for hypertension, diabetes mellitus, hypercholesterolemia, and heart diseases as risk factors for recurrent stroke events is considered effective because it is easy, simple, low cost, sensitive, and does not cause additional suffering for patients.

**Conclusion:** A practical and non-invasive method for early detection and monitoring of risk factors may reduce the risk of stroke recurrence among stroke survivors.

**Keywords**
Digital sensor, quality of care, risk factors, recurrent stroke.
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Introduction

Stroke is defined as an infarction of brain, spinal cord, or retinal cell death attributable to ischemia, based on pathological, imaging, or other objective evidence of cerebral, spinal cord, or retinal focal ischemic injury in a defined vascular distribution; or clinical evidence of cerebral, spinal cord, or retinal focal ischemic injury based on symptoms persisting ≥ 24 hours or until death, and other etiologies are excluded. In 2013, strokes contributed to 1 out of 20 deaths in the United States. Stroke affects one person in every 40 seconds and it claims one life every 4 minutes.

There are two types of risk factors for stroke: modifiable and non-modifiable. Non-modifiable risk factors include age, gender, low birth weight, race, and genetic factors. Modifiable risk factors include hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, and heart disorders. Patients who have suffered from strokes are at risk of stroke recurrence or relapse with a cumulative risk of 39.2%. Approximately 13% of patients with stroke are affected by recurrent stroke within the first year after the initial event. A systematic review reported that recurrent stroke was the major reason for hospital re-admission among patients with ischemic stroke within the first 30 days and 1 year following the initial event, (33% and 26.3%, respectively). Hospitals are currently challenged to reduce preventable hospital re-admission for cost retrenchment and improvement of service quality. Furthermore, the incidence of recurrent stroke is significantly associated with increased mortality and morbidity because it results in greater neurological deficits than initial stroke, which lead to longer hospital stays and higher cost of care.

Various prevention and behavior change programs have been implemented. However, these have not significantly reduced the prevalence of recurrent stroke and re-admission rate. Health professionals are facing a challenge to provide health education to the community and make a breakthrough to improve awareness about stroke or recurrent stroke, especially awareness among those who possess higher risk factors. Utilization of advanced technology, such as digital sensors, (a non-invasive device) is among the breakthroughs in detecting the risk of disease for more effective prevention. Unlike invasive procedures, sensor technology undoubtedly facilitates health professionals in detecting risk factors of stroke in patients in an easy and pain-free manner.

To the best of the author’s knowledge, there has not been a study conducted that systematically reviews the literature addressing early detection of risk factors of stroke through the use of digital sensors in order to establish proper practice guidelines in developing non-invasive devices for identifying the risk factors for stroke recurrence.

Methods

Search strategy

The search strategy included the following terms: 'risk factor of stroke', 'post-stroke', 'recurrent stroke', 'stroke prevention', 'detection', 'digital sensor', 'non-invasive', and 'nursing'. The chronological search range was between 1 January 2018 and 31 August 2018. Databases used for searching literature included: EBSCO, Elsevier ScienceDirect, ProQuest, Springer link, PubMed, MEDLINE, PLoS, and the Journal of Community Nursing.

The search process resulted in 92 articles which matched the keywords. These articles were then filtered according to full text and publication year between 2011 – 2018 which resulted in 49 articles. These 49 articles were then reviewed based on titles matching the use of digital sensors (non-invasive) for early detection of risk factors for recurrent stroke and resulted in 16 articles. Finally, these 16 articles were filtered based on inclusion and exclusion criteria, (see below) and resulted in 10 articles. The search process on the databases is shown in Figure 1.

Critical appraisal was later performed according to the study design of the articles. The Critical Appraisal Skills Program (CSAP) was used for analysis.

Ten articles were analyzed through data extraction. Variables acquired through data extraction were: authors name(s), year of study and publication, intervention method, and study findings. All the items were included in the table of data extraction. We used the Cochrane Collaboration free software called Review Manager (RevMan version 5.3) which is useful for analyzing results and generating forest plots and risk-of-bias. The results of bias assessed are shown in Figure 2.

Inclusion criteria

1. Stroke survivor.
2. Finding: Patient identified as having a high risk factor for recurrent stroke.
3. Include examination of stroke risk factors using digital sensors.
4. Language and publication date: published in English language between 2011 and 2018.
5. Study design: Randomized Controlled Trial, meta-analysis, cohort study, survey and case report.

Exclusion criteria

This study that did not address the use of sensory non-invasive devices to detect risk factor of stroke and nursing intervention in educating patients to prevent stroke recurrence.

Results

The characteristics of the selected studies are outlined in Table 1. The systematic review revealed risk factors of recurrent stroke that included hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, and heart disorders. Those risk factors were detected by a non-invasive device consisting of various sensors and tools that reduced the patient’s pain during examination. The review also found that the nurse is part of the multidisciplinary team that provides care for patients with stroke. One of nurse’s roles and functions is to promote independence.
Records identified through database searching (n = 92)

Records after duplicates removed (n = 92)

Records screened (n = 92)

Records excluded (n = 43)

Full-text articles assessed for eligibility (n = 49)

Full-text articles excluded, with reason 'no human research' (n = 33)

Studies included in qualitative synthesis (n = 16)

Articles included in the systematic review (n = 10)

Figure 1. Result of a systematic search in databases related to use of digital sensors (non-invasive) for early detection of risk factors for recurrent stroke.

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Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias

Figure 2. Risk of bias summary: review authors’ judgements about each risk of bias item for each included study used RevMan 5.3.
Table 1. Description of studies included in the systematic review.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study design</th>
<th>Device used</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>Cohort Study</td>
<td>Computed Tomography Coronary Angiography (CTCA)</td>
<td>CTCA as a first-line diagnostic modality for diagnosis of suspected angina and magnetic resonance perfusion provided significant contribution in detection of cardiac lesions.</td>
</tr>
<tr>
<td>10</td>
<td>Experimental</td>
<td>Biosensor was fabricated using electrospun polyaniline nanofiber</td>
<td>Biosensor that implemented nanofibers was claimed to be accurate in identifying blood cholesterol level in comparison with the results of invasive tests.</td>
</tr>
<tr>
<td>11</td>
<td>Experimental</td>
<td>The Cu-graphene sheets electrode</td>
<td>Cu-graphene sheet electrode was able to quickly detect blood glucose level with highest stability, sensitivity and selectivity.</td>
</tr>
<tr>
<td>12</td>
<td>Experimental</td>
<td>FET sensor for cholesterol detection</td>
<td>Sensor-based FET was able to detect cholesterol levels easier and more practical.</td>
</tr>
<tr>
<td>13</td>
<td>A Randomized, Controlled Trial</td>
<td>Non-invasive cardiac-event by an accredited cardiac electrocardiology laboratory</td>
<td>Monitoring of cardiac activity for 7 days following acute stroke was effective in detecting paroxysmal atrial fibrillation and early anticoagulation.</td>
</tr>
<tr>
<td>14</td>
<td>Experimental</td>
<td>Glucose Enzyme biosensors</td>
<td>The glucose enzyme sensor demonstrated sensitivity that has never occurred before in detecting blood glucose level.</td>
</tr>
<tr>
<td>15</td>
<td>Experimental</td>
<td>G/PVP/PANI-modified paper-based biosensor</td>
<td>Development of a sensitive, accurate and inexpensive biosensor is critical in the detection of early stage biomarkers of a disease, including cholesterol.</td>
</tr>
<tr>
<td>16</td>
<td>Cohort Study</td>
<td>A Non-Invasive Blood Pressure Measurement using Smart Android</td>
<td>Sensor with C8051F410 mixed-signal 8-bit MCU chip was used for measurement of blood pressure through the fingertip.</td>
</tr>
<tr>
<td>17</td>
<td>Experimental</td>
<td>Fluorogenic sensors</td>
<td>Fluorogenic sensors capable of detecting Fe²⁺ spatiotemporally in biological systems to identify symptoms of ischemic stroke.</td>
</tr>
<tr>
<td>18</td>
<td>Experimental</td>
<td>Model-View-Controller software architecture pattern</td>
<td>This biometric device was more efficient in detecting blood pressure and Wi-Fi connectivity allowed patients to directly monitor it through their smart phone.</td>
</tr>
</tbody>
</table>
of the patient in performing self-screening, prevention, disease management and rehabilitation. Advancing technology would facilitate a nurse in identifying risk factors of stroke.

Utility of digital sensors to detect hypertension. Studies have suggested that hypertension is the main risk factor for stroke, though it is also the easiest to modify if the affected person is willing to adopt a healthier lifestyle. The mean blood pressure of the affected person ranges from systolic pressure $\geq 140$ mmHg or diastolic pressure $\geq 90$ mm Hg. Prevalence of hypertension in patients with ischemic stroke approaches 70%\(^7\). Hypertension treatment is described as the most crucial intervention in secondary prevention of ischemic stroke. The risk of ischemic stroke is significantly associated with blood pressure (BP) with systolic blood pressure (SBP) as low as 115 mmHg. It is also directly correlated with the patient's blood pressure monitoring up to 4 times a day. Therefore, regular monitoring will assist in providing appropriate medication\(^7\).

People with hypertension require a blood pressure measurement device to monitor their hypertension status. However, they also need to access a health facility just to measure their blood pressure and the measurement is performed by a trained staff, such as a nurse or other health professional. It is considered a time consuming activity by patients who could otherwise be more productive. Although they may be able to purchase it, the device is mostly magnetically based and applies an indirect method of blood pressure detection using Korotkoff sounds. The method is also difficult to conceptualize and there are certain procedures that require careful attention, including proper cuff positioning which, significantly affects the measured parameter. Furthermore, the device also possesses built-in ambivalence in which the measurement of systolic and diastolic pressure from an empirically measured mean of pressure is also influenced by user's hearing. Therefore, its use is rather less effective and efficient\(^8\). Such deficiencies have led to the development of a blood pressure measurement device that utilizes automatic measurement features. It is easy to use, only requiring a finger tap and the sensor will automatically measure the blood pressure with a sensitivity matching the user's condition. Measurement of blood pressure through such a digital sensor also offers advantage that it enables the patient to monitor his own blood pressure at any time\(^9\).

Utility of digital sensor to detect blood glucose. Elevation of blood glucose levels over the normal range indicates diabetes mellitus which is an independent risk factor for stroke. Most people with diabetes are also affected by hypertension, hypercholesterolemia and are overweight. These conditions increase the risk for stroke recurrence. Even though diabetes is a treatable disease, uncontrolled diabetes may increase the risk for stroke\(^1\). Control of blood glucose levels heavily depends on blood glucose monitoring. Patients with type 1 or type 2 diabetes are recommended to check his or her blood glucose level up to 4 times a day\(^1\). The measurement is generally performed by using a finger-prick glucose meter. The test will reveal the patient's blood glucose level which is required to calculate the insulin dose every day. The disadvantage of this measurement is that it causes pain when the finger is pricked. In addition to the impracticality of glucose meter device, there is also a risk for infection associated with tissue injury and damage of tissue associated with puncture wounds over a long period. Several factors may cause the patient to neglect blood glucose monitoring\(^1\). This reality led to the invention of non-invasive technologies for blood glucose monitoring. Advancing technology allows exploration of non-invasive blood glucose monitoring through the use of a practical digital sensor that is portable and pain-free for the user. Infrared spectroscopy is the method used by a type of sensor which is highly sensitive to blood glucose levels. The patient only needs to place a finger on the sensor and it will operate according to user's physiological condition, metabolism, and circulation. This device requires reliability and must be calibrated to ensure the accuracy of the blood glucose result\(^1\).

Utility of digital sensor to detect cholesterol. People with hypercholesterolemia are at higher risk of stroke. A considerable amount of cholesterol in the blood might develop and lead to coagulation, atherosclerosis, and blood flow obstruction which causes stroke. Moreover, low levels of High Density Lipoprotein, (HDL “good” cholesterol) is recognized as a risk factor for stroke in males\(^1\). Modification of primary serum lipid biomarkers, such as low-density lipoprotein cholesterol (LDL-C), might be implemented as a strategy for reducing risk of secondary stroke among patients with TIA or ischemic stroke. Considering that hypercholesterolemia is associated with arteriosclerosis, hypertension, and myocardial infarction, identifying cholesterol levels is imperative for establishing a clinical diagnosis. A diagnostic test is required to identify cholesterol levels. Most hospitals currently still apply an invasive or traditional procedure that includes glass, ceramic and polymer and the results require waiting time. Therefore, a device to detect cholesterol levels through a digital sensor which is pain-free with rapid and accurate results is currently being developed\(^1\).

Development of a sensitive, accurate, and inexpensive biosensor will facilitate the filtering of biomarkers of certain diseases. Cellulose filter paper has recently been invented for sensory applications at a very low cost. The paper-based biosensor offers several advantages including biocompatibility, low cost and disposability\(^10\). In addition, amperometric biosensors that incorporate analytical devices are capable of converting concentrations of electrical signals which are integrated with biological sensors. Hence, portable biosensors are user-friendly, possess high specificity, and are currently utilized in multidisciplinary fields, including pharmacy, nursing, medicine and physiotherapy. The portable biosensors allow easy detection of cholesterol levels without any associated pain and require shorter times to produce the result. A sensitive, selective, reliable and inexpensive cholesterol sensing device is presently being developed for clinical use in measuring cholesterol levels which allows independent monitoring by the user at home\(^12\).

Utility of digital sensors to detect cardiac disorders. Heart attack occurs when plaque accumulation causes a blockage in blood vessels supplying the heart. Most stroke cases are also primarily caused by an accumulation of plaque that causes a
blockage in blood vessels within the brain. Electrocardiography (ECG) may be employed to identify heart disorders and its use is still very widespread. However, the result requires interpretation by health professionals, even if the patient is able to afford the device. A study reported that 1 out of 5 patients with ischemic stroke or TIA had a medical history of atrial fibrillation (AF) or indicated that they were affected by AF, according to a 12-lead ECG, putting at risk in the future. Early detection of AF may lead to appropriate treatment and offer more cost effective care in health system.

Discussion

Recurrent stroke is an event that occurs after an initial stroke attack. The American Stroke Association (ASA) claims that the average risk of stroke recurrence after ischemic stroke or TIA (transient ischemic attack) is 3–4%. Following recuperation from stroke, most patients prioritize rehabilitation and recovery programs while neglecting efforts for secondary prevention. Secondary prevention is fundamental to prevent stroke recurrence as it may result in a more debilitating impact than the initial stroke.

Risk factors of recurrent stroke are similar to those of primary stroke and include modifiable and non-modifiable factors. Secondary prevention refers to all efforts made to prevent recurrent stroke. Secondary prevention involves all attempts which address modifiable risk factors. Secondary prevention consists of risk factor management, intervention to resolve vascular obstruction, anti-thrombotic therapy for cardio embolic stroke, and antiplatelet therapy for non-cardio embolic stroke. Nurses play an important role as educators in secondary prevention by providing health information for controlling risk factors. Studies addressing knowledge about the risk of impending stroke had been focused on the community as a whole. A study evaluating knowledge about risk factor in patients at high risk revealed that only 42% of patients with a history of stroke were aware of their own risk of stroke recurrence and only 27% of them reported it to a physician. The study also identified a low level of awareness of risk of recurrence among high risk participants (41%), especially those with a medical history of hypertension, diabetes mellitus, hypercholesterolemia and heart disorders.

Assessment of independent risk factors which trigger recurrent stroke such as hypertension, diabetes mellitus, hypercholesterolemia and heart disease are resources intensive. The frequent measurement of blood glucose is an essential part of recurrent stroke monitoring. Despite the fact that almost all the commercially successful blood glucose monitoring devices are invasive, there is an immense need to develop non-invasive monitoring devices that will alleviate the pain and suffering of patients associated with the frequent pricking of skin needed to obtain blood samples for glucose testing. These issues may cause the patient to neglect blood glucose monitoring in health facilities. Therefore, all health professionals, including nurses, are required to be involved in monitoring the patient’s recovery process, including providing motivation and involvement in the development of health devices that contribute to an effective and efficient service for the patient. Current health devices are primarily developed based on a non-invasive concept, which aims to provide comfort during the diagnostic process and are more practical than invasive procedures.

A glucose sensor with ultrahigh sensitivity and a rapid response time was constructed using a PtNP/ PANI hydrogel heterostructure for non-invasive glucose monitoring. Studies have shown that the glucose sensors composed of the PtNP/PANI hydrogel heterostructure exhibited unprecedented performance with ultrahigh sensitivity, fast response, and a very low detection threshold and has great potential for use in applications relating to medical diagnosis. Another study about non-invasive glucose monitoring was conducted by Luo et al. (2011). In this study, a novel amperometric glucose sensor based on Cu decorated graphene sheets sensor the advantages of ease of fabrication, low cost, good reproducibility and perfect specificity to glucose, so is a potential candidate for routine glucose analysis.

Similar to glucose, methods of monitoring non-invasive hypercholesterolemia are being developed. Ruecha et al. (2014) fabricated a novel nano composite based on G/PVP/PANI using a paper-based cholesterol biosensor that might be an alternative tool for cholesterol screening in medical diagnosis due to its simplicity, low cost, disposability and portability. Other media such as field-effect transistors have a wide linear range and high sensitivity for detection of cholesterol which suggests that this cost-effective process can lead to portable, reliable and real-time cholesterol detection. In addition, amperometric cholesterol biosensors using a layer-by-layer adsorption technique onto electrosyn polyaniline nanofibers has been used to measure cholesterol concentration.

Non-invasive monitoring of heart disease as a recurrent stroke risk factor was conducted by Higgins et al. (2013) using the Novacor R-test Evolution 3 device to detect atrial fibrillation after ischemic stroke. These method was effective because it enhances detection of paroxysmal atrial fibrillation and early anti-coagulation. Non-invasive blood pressure measurement using android smart phones and web applications offer solutions for patients, relatives, doctors and nurses to monitor blood pressure as a predictor of recurrent stroke.

However, most non-invasive technologies, especially digital sensors that detect blood pressure, blood glucose level, cholesterol level and cardiac disorders are still under development. There are various non-invasive technologies outlined in this study and the volume of new studies for this type of non-invasive concept increases yearly. The current situation requires constant updates of available technology. With the advancement of technology, it becomes challenging for the health workers to develop a strategy for monitoring risk factors recurrent stroke in a comprehensive manner. To that end, this paper provides an overview of currently available non-invasive digital sensors for monitoring blood pressure, blood glucose level, cholesterol level and heart disorders. Furthermore, the adoption of non-invasive monitoring technology is increasing because it is easy to use, low cost, sensitive, and does not cause pain in the patients.
A practical test to detect risk factors of recurrent stroke is expected to be used as an initial guideline to promote a healthier lifestyle and behavior among patients. Individual resolve should be taken into consideration to increase the success rate of the stroke patient’s behavior in monitoring and managing risk factors as well as modifying their lifestyle in order to prevent stroke recurrence which, in turn, improves his or her quality of life. A previous article revealed that non-invasive methods of diagnostic tests should always be accompanied by an invasive method, specifically when identifying lesions in acute coronary syndrome and also in major diagnostic tests in order to prevent gaps in results from both methodologies. However, several articles reported that application of non-invasive devices such as digital sensors offer ease of use, low cost, sensitivity, and do not cause suffering during detection of risk factors of stroke recurrence, including hypertension, diabetes mellitus, hypercholesterolemia and cardiac disorders. Hence, development of non-invasive devices with valid predictive results progresses in order to drastically reduce invasive procedures that may cause pain for patients, especially in diagnostic tests for heart failure, kidney failure and vascular disorders. Nevertheless, non-invasive devices have their weakness, and there are no digital sensors currently in use for the detection of hypertension, diabetes mellitus, hypercholesterolemia and heart disorders together.

It becomes a challenge for health workers to develop a strategy for monitoring risk factors for recurrent stroke in a comprehensive manner. On the other hand, the patient is required to purchase all four devices to identify risk factors of recurrent stroke. Yet, this self-screening ability will provide confirmation for patients who are at risk of stroke recurrence so they can follow it up with appropriate prevention measures, including improving lifestyle and accessing health provision to manage and mitigate the risk of recurrence. Recognizing changes in and development of risk factors in patients may inform their decision to access hospital treatment. Consequently, a non-invasive device capable of detecting the four risk factors of stroke recurrence in a single test is expected to be developed in the future. Moreover, such an all-in-one device would be able to calculate cumulative risk of recurrent stroke.

**Conclusion**
The incidence of recurrent stroke is quite high and causes rehospitalization of patients. There are several factors that can cause recurrent stroke, including hypertension, hyperglycemia, hypercholesterolemia and heart disease especially atrial fibrillation. It is very important to monitor these factors. With the development of technology, the potential use of non-invasive monitoring for risk factors for recurrent stroke events is considered effective because it is easy to use, low cost, sensitive, and does not cause suffering in patients. There is currently no non-invasive monitoring that assesses all these factors simultaneously. The challenge for health workers is to develop a means of non-invasive monitoring of risk factors for the incidence of recurrent stroke in a comprehensive manner.

**Data availability**

**Underlying data**
All data underlying the results are available as part of the article and no additional source data are required.

**Extended data**

Open Science Framework: PRISMA checklist, https://doi.org/10.17605/OSF.IO/DA3CK

Data are available under the terms of the Creative Commons Zero “No rights reserved” data waiver (CC0 1.0 Public domain dedication).

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10. Shin YJ, Kameoka J: Amperometric cholesterol biosensor using layer-by-layer


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