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Stroke: New Risk Factors and Improved Patient Care

Sleep Disturbances as a Risk Factor for Stroke

Sleep, a vital process of human being, is carefully orchestrated by the brain and consists of cyclic transitions between rapid eye movement (REM) and non-REM (NREM) sleep. Autonomic tranquility during NREM sleep is characterized by vagal dominance and stable breathing, providing an opportunity for the cardiovascular-neural axis to restore homeostasis, in response to use, distress or fatigue inflicted during wakefulness. Abrupt irregular swings in sympathovagal balance during REM sleep act as phasic loads on the resting cardiovascular system. Any causes of sleep curtailment or fragmentation such as sleep restriction, sleep apnea, insomnia, periodic limb movements during sleep, and shift work, not only impair cardiovascular restoration but also impose a stress on the cardiovascular system. Sleep disturbances have been reported to play a role in the development of stroke and other cardiovascular disorders. This review aims to provide updated information on the role of abnormal sleep in the development of stroke, to discuss the implications of recent research findings, and to help both stroke clinicians and researchers understand the importance of identification and management of sleep pathology for stroke prevention and care.

Keywords: Sleep initiation and maintenance disorders; Sleep; Sleep apnea syndromes; Stroke; Cardiovascular system; Homeostasis

Introduction

Stroke incidence and early stroke mortality have been decreasing, at least in developed countries, although stroke remains one of leading causes of death and significant disability worldwide.[1-5] Identification and active modification of risk factors, as well as progress in acute stroke care, underlie the improvements in stroke statistics. Modifiable risk factors such as high blood pressure, hyperlipidemia, diabetes, smoking, physical inactivity, and unhealthy diet are responsible for 90% of the risk of stroke.[6,7] However stroke incidence has not dropped significantly in young adults, and is still soaring in low and middle income countries.[2,3,8] The absolute numbers of stroke victims and resulting deaths, and the associated societal burden are great and even increasing.[2] Insufficient modification of the established risk factors, or the ongoing effects of under-recognized risks, might explain the high global burden of stroke. Recently, the role of sleep pathology in the development of cardiovascular and metabolic diseases has been highlighted by experimental and observational studies.[9-15]

Sleep is an indispensable part of life, as with feeding and reproduction, all animal species require sleep. Humans sleep almost one-thirds of their lifetime, which is similar in industrialized and in pre-industrial societies.[16,17] Sleep, although characterized by quiescence and diminished responsiveness, is not a simple state of rest, but rather a cyclic state of periodic transitions between rapid-eye-movement (REM) and non-REM (NREM) sleep, which are precisely regulated by the central nervous system.[18] Along with the brain and other organs or physiological streams, the cardiovascular system achieves homeostatic restoration during sleep, mainly through autonomic circulatory control.[19] For example, the decrease in blood pressure during sleep, "dipping," is a key biomarker of cardiovascular health, secondary to changes in activity and posture and also under the influence of sleep and circadian rhythms.[20,21] During NREM sleep, the largest portion (up to 80%) of normal adult sleep, the autonomic system is stabilized with vagal dominance, reduced sympathetic tone, and heightened baroreceptor gain, contributing to a significant reduction in blood pressure and heart rate, with the greatest drop occurring during slow wave sleep.[21-24] This salutatory milieu makes it easy for the cardiovascular system to maintain homeostasis. In contrast, REM sleep—occupying about 20% of total sleep—is dominated by marked fluctuations in sympathovagal balance (irregularly peaking sympathetic surges against a background of tonic vagal inhibition), which lead to abrupt changes in blood pressure and heart rate.[9,19,22,24] A compromised cardiovascular system is at risk for pathological events such as myocardial ischemia or arrhythmias during REM sleep. Sleep thus acts as a gatekeeper through cyclic oscillations between NREM and REM sleep, switching between autonomic tranquility and turmoil.

Any causes of sleep curtailment, including sleep restriction, insomnia, and shift work, are likely to impair cardiovascular restoration through a reduction in cardioprotective stable NREM sleep. Sleep fragmentation, conventionally defined by cortical EEG arousals, is a universal feature of almost all sleep disorders, including sleep apnea, insomnia, periodic limb movements during sleep (PLMS) and narcolepsy, and is associated with overshoots in sympathetic activity.[25,26] Even if REM sleep is preserved, the greater the sleep fragmentation, the farther the sympathovagal modulation is tilted toward sympathetic dominance.[27] Blood pressure regulation during the biological night (the usual sleep time) is uniquely related to cardiovascular risk, including the risk of stroke.[28-30] Non-dipping—loss of the typical blood pressure drop during sleep—is associated with a host of poor cardiac, neurological, metabolic, and renal outcomes.[31-36] Sleep fragmentation causes non-dipping.[37-40] Non-dipping is common in older adults and is associated with an increased risk of stroke.[41-43] Reduced dipping is associated with brain atrophy, worse functional status, and lower daytime cerebral blood flow.[44,45]

The deleterious effects of sleep disturbances go far beyond autonomic circulatory derangement. Common sleep disorders such as sleep apnea, insomnia, and PLMS activate multiple mechanisms including intermittent hypoxia-reoxygenation injury, inflammation, insulin resistance, hypothalamic-pituitary-adrenal axis activation, hemodynamic swings, cardiac arrhythmia, and hypercoagulability, all of which have the potential to provoke cardiovascular diseases (Figure 1).[9,46]

However, compared with studies on well-established risk factors, research on the role of sleep pathology in the development of cardiovascular diseases, including stroke, has largely been observational or experimental.[13,47-58] To complicate matters, recent randomized trials have failed to determine the beneficial effect of positive airway pressure therapy in the secondary prevention of cardiovascular events or mortality in sleep apnea.[59-61] However, serious flaws are pervasive in these studies, including poor use of therapy. This review aims to (1) provide an update of the available information regarding the role of sleep disturbances on the development of stroke; (2) discuss the implications of recent clinical trials and observational studies; and (3) help both stroke clinicians and researchers understand the importance of identification and management of sleep pathology for primary prevention in the general and stroke-prone populations, and for the care of acute and chronic stroke.

Obstructive sleep apnea

Obstructive sleep apnea (OSA) is characterized by repetitive cessations or reductions in airflow caused by complete or partial upper airway collapse (Figure 2). The prevalence of moderate-to-severe OSA in the adult general population is 9% to 14% in men and 4% to 7% in women,[62-65] increasing with age,[66] and even higher in a recent study (49.7% in men, 23.4% in women).[67] Measurement methods and scoring criteria heavily impact reported prevalence rates. Nevertheless, the prevalence and incidence of OSA is clearly increasing, driven by the aging of societies and the obesity epidemic.[68] Four decades after a report on the high prevalence of hypertension in pediatric and adult OSA,[69] numerous experimental and observational studies have provided evidence that OSA promotes the development of cardiovascular diseases, including stroke.[9,12,46,70]

Links between OSA and stroke

OSA creates a substrate for stroke vulnerability, and is particu-

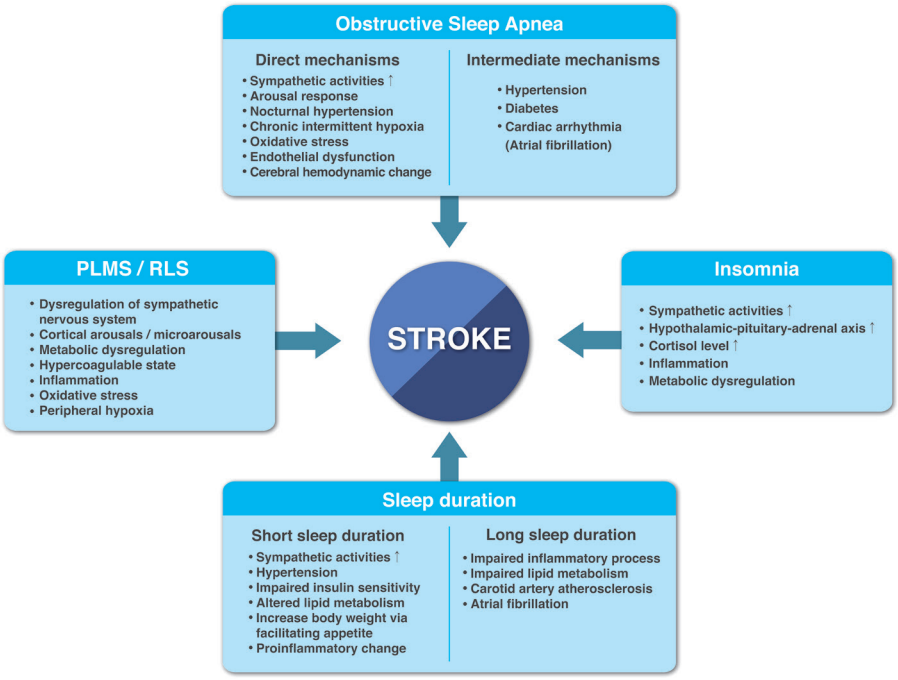

Figure 1. The mechanisms of sleep disturbances contributing to the development of stroke. PLMS, periodic limb movements during sleep; RLS, restless legs syndrome.

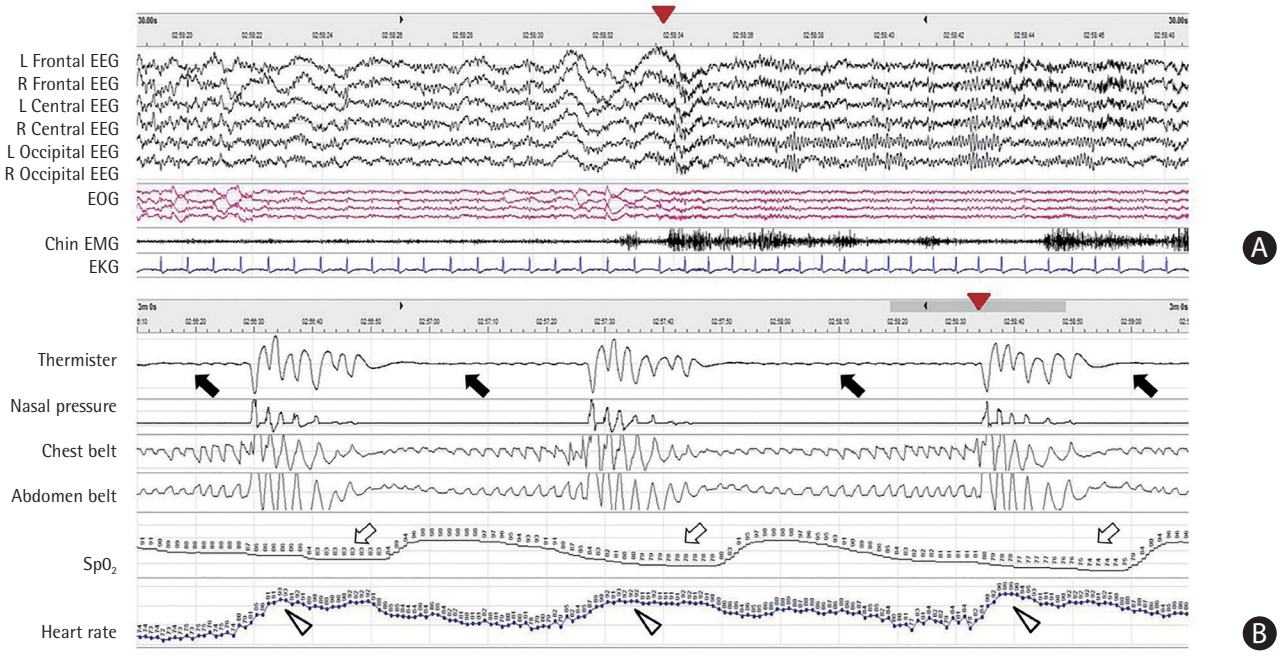

Figure 2. Snapshot of recurrent respiratory events in obstructive sleep apnea. (A) Electroencephalography (EEG) plots for 30-second epoch. Respiratory arousal (closed arrowhead in panel A) occurs at the end of obstructive sleep apnea (closed arrowhead in panel B) in stage 2 rapid-eye-movement (REM) and non-REM sleep. The closed arrowheads on panel A and B indicate the same time. (B) Respiratory plots for three-minute epoch. Repetitive cessations of airflow (closed arrows) despite ongoing respiratory movements of the chest and abdominal belt are typical features. Obstructive sleep apnea is accompanied by decreased oxygen saturation (open arrows) and increased heart rate (open arrowheads). L, left; R, right; EOG, electrooculography; EMG, electromyography; EKG, electrocardiogram; SpO_2, peripheral oxygen saturation.

larly hostile to brain function. Exposure to intermittent hypoxia in rodents results in impaired executive function, excessive sleepiness, and sensitivity to sleep deprivation.[71-74] There is evidence of neuronal injury in the hippocampus,[75,76] the basal forebrain,[77] and the wake-promoting catecholaminergic system.[78] The mediating mechanisms include free radical injury, lipid peroxidation, induction of nitric oxide synthase, platelet activation, and apoptosis.[79-81] However, oxidative stress, especially modest hypoxia, may have a protective effect on the brain and cardiovascular system by activating gene programs that induce vascular remodeling as well as other protective responses; thereby, engendering resilience in the brain (known as ischemic preconditioning).[82]

OSA is related to the surrogate index of stroke. Moderate-to-severe OSA is associated with silent ischemic changes, including white matter changes and lacunae as well as cerebral microbleeds.[83-86] Carotid and intracranial atherosclerosis are also accelerated in OSA.[87,88] It is unclear whether continuous positive airway pressure (CPAP) has a therapeutic effect on these changes.[89]

Hypertension and insulin resistance might mediate the development of stroke in OSA. Moderate-to-severe OSA is significantly associated with prevalent and incident hypertension in a severity-dependent manner,[90,91] and is highly prevalent in patients with resistant hypertension.[92] Effective CPAP therapy, alone or in addition to antihypertensive medication, significantly reduces blood pressure.[93-95] OSA may also increase the risk for development of type 2 diabetes by mechanisms such as increased insulin resistance and high cortisol secretion.[12,96] In a 6-month parallel trial, the CPAP group achieved a greater decrease in HbA1c (–0.4%; 95% confidence interval [CI], –0.7% to –0.04%) than the control group.[97] Continuously supervised CPAP therapy (7.92 hr/night) improved glycemic control and insulin resistance.[98] However, the CPAP effect on glycemic control is less consistent than its effect on blood pressure. Concomitant obesity might have a stronger effect than OSA, not mitigated by CPAP therapy.

OSA is also associated with the risk for cardioembolism. Nearly 40% of symptomatic atrial fibrillation events are seen between midnight and 8:00 AM.[99] People with OSA have four times the odds of atrial fibrillation (odds ratio [OR], 4.02; 95% CI, 1.03 to 15.74).[100] Nocturnal oxygen desaturation is an independent risk factor for new onset atrial fibrillation.[101] In a recent cohort study of 6,841 patients, OSA diagnosis and severity were associated with atrial fibrillation (hazard ratio [HR], 1.55; 95% CI, 1.21 to 2.00) during a follow-up of 12 years.[102] Furthermore, OSA may potentiate the risk of cardioembolism or stroke in patients with atrial fibrillation.[103,104] Several observational studies found an improvement or resolution of cardiac arrhythmia and atrial fibrillation after CPAP therapy.[105,106]

In addition, sleep apnea is associated with inflammation,[107-110] endothelial dysfunction,[111,112] hypercoagulability,[113-115] and cerebral hemodynamic changes.[116-118] The overall findings suggest that OSA contributes to the development of stroke through various mechanisms downstream to intermittent hypoxia, sleep fragmentation, and hemodynamic swings.[9,12,46,70]

Observational findings

Sleep apnea is exceedingly common in the acute stroke setting, present in 50% to 70% of subjects with acute stroke or transient ischemic attacks, which is a higher frequency than observed in control groups.[119-122] However, OSA and stroke share risk factors such as male sex, obesity, old age, hypertension, and smoking.[62,65,66,68] An independent association between the two conditions was supported by large scale epidemiological studies including the Sleep Heart Health Study and the Wisconsin Sleep Cohort Study.[48,123] In these studies, OSA with an apnea-hypopnea index (AHI) ≥20/hr or >11/hr was related to prevalent stroke, with an OR of 4.31 (95% CI, 1.31 to 14.15) and 1.58 (95% CI, 1.02 to 2.46), respectively, when adjusted for age, sex, weight, blood pressure, smoking, and other confounders. Prospective cohort studies in clinical or general populations followed, and the major findings are summarized in Table 1.[47-49,124-128]

In the first study on the temporal relationship between OSA and stroke in the general population (from the Wisconsin Sleep Cohort), the causal association was attenuated (OR, 3.08; 95% CI, 0.74 to 12.81) when adjusted for age, sex, and body mass index.[48] The younger age of the cohort (mean age, 47±8 years old) and a low incidence of stroke (1.3 per 1,000 person-years) probably weakened the statistical power. In the Sleep Heart Health Study (n=5,422; stroke incidence, 4.4 per 1,000 person-years), men with moderate-to-severe OSA (AHI >19/hr), but not women, had a higher risk for ischemic stroke during follow-up (median, 8.7 years; HR, 2.86; 95% CI, 1.1 to 7.4). The lack of association in women was explained by insufficient statistical power (lower stroke incidence in women); the relatively shorter duration of OSA exposure (due to the later, usually postmenopausal, onset in women);[129] the higher rate of OSA progression along with aging during the follow-up, leading to a considerable probability of misclassification (OSA vs. control, or OSA severity); and the stronger effects of well-known vascular risk factors.[49] For elderly people of both sexes (aged 70 to 100 years, n=394), the risk of incident stroke was significantly higher for severe OSA (AHI ≥30/hr; HR, 2.52) throughout a 6-year period of observation, independent of

Table 1. Studies of obstructive sleep apnea at risk for stroke

Study	Design	Number	Group	Primary outcome*	Risk factor adjustment
Arzt et al. (2005)[48]	General population cohort, follow-up at every 4 yr	1,189	AHI >20 vs. <5	Incident stroke OR, 3.08 (0.74–12.81)	Age, sex, and BMI
Redline et al. (2010)[49]	General poulation cohort, (median) 8.7 yr follow-up	5,422	AHI >19 vs. <4	Incident stroke Men: HR, 2.86 (1.10–7.39) Women: HR, 1.21 (0.65–2.24)	Age, BMI, smoking, blood pressure, antihypertensives, diabetes mellitus, and race
Marin et al. (2005)[125]	Clinic (OSA) and general population (control) cohort, 10.1 yr follow-up	1,010 men	Untreated severe OSA (AHI ≥30 or AHI 5–30 with severe daytime sleepiness) vs. AHI <5	Incident composite cardiovascular events Non-fatal: OR, 3.17 (1.12–7.51) Fatal: OR, 2.87 (1.17–7.51)	Age, cardiovascular disease, diabetes mellitus, hypertension, lipid disorders, smoking, alcohol, blood pressure, glucose, and lipid levels
Munoz et al. (2006)[126]	Clinic cohort, (mean) 4.5 yr follow-up	394	AHI >30 vs. 0–29	Incident stroke HR, 2.52 (1.04–6.10)	Sex (distribution of other risk factors were balanced between the two groups)
Yaggi et al. (2005)[47]	Clinic cohort, (median) 3.4 yr follow-up	1,022	AHI >5 vs. AHI <5	Incident stroke or death of any causes HR, 1.97 (1.12–3.48)	Age, race, sex, smoking, alcohol, BMI, atrial fibrillation, hypertension, and lipids
Yeboah et al. (2011)[128]	General population cohort, (mean) 7.5 yr follow-up	5,338	Physician diagnosed OSA vs. normal control	Incident cardiovascular events HR, 2.16 (1.30–3.58) All-cause mortality HR, 2.71 (1.45–5.08)	Age, gender, race/ethnicity, smoking, diabetes, total cholesterol, high-density lipoprotein, triglyceride, BMI, alcohol, benzodiazepine/statin/antihypertensive use
Young et al. (2008)[127]	General population cohort 18 yr follow-up	1,522	AHI >30 vs. AHI <5	Cardiovascular mortality HR, 5.2 (1.4–19.2) All-cause mortality HR, 3.8 (1.6–9.0)	Age, sex, BMI, smoking, alcohol, total cholesterol, and sleep duration

AHI, apnea-hypopnea index; OR, odds ratio; BMI, body mass index; HR, hazard ratio; OSA, obstructive sleep apnea.
*Adjusted OR or HR (95% confidence interval).

other vascular risk factors.[126]

Prospective observational studies of clinic-based cohorts, assessing composite cardiovascular events as a primary endpoint, also suggested a role for OSA in the development of stroke.[124,125] Peker et al.[124] reported an independent association of OSA with cardiovascular events in a small community sample of men (age, 30 to 69 years old; n=182) free from prevalent cardiovascular diseases, hypertension, and diabetes. During the 7-year follow-up, the OR for people with OSA having cardiovascular diseases (including stroke) was 4.9 (95% CI, 1.8 to 13.6), and effective treatment of OSA significantly reduced the risk (OR, 0.1; 95% CI, 0.0 to 0.7). The effect of treatment, as well as the contribution of OSA to cardiovascular event incidence, were demonstrated in a subsequent long-term observational study of a clinical population (mean observation period, 10.1 years; n=1,656).[125] The group of subjects with untreated severe OSA (AHI ≥30/hr or 5 to 29/hr with severe sleepiness) had a higher hazard for fatal and non-fatal cardiovascular diseases (HR, 2.87 and 3.17, respectively), compared with age- and body mass-matched controls. With an average nightly use of CPAP for at least 4 hours, the risk of incident cardiovascular events among subjects with severe or symptomatic OSA was comparable to that of controls or simple snorers (AHI <5/hr). The cardiovascular effects of OSA are not limited to subjects with a severe burden of OSA. A prospective observational study in a clinical population (aged ≥50 years; n=1,022) free from myocardial infarction or stroke at study entry, found that the presence of OSA (AHI ≥5/hr) increased the risks for outcome events (stroke or death from any cause, HR, 1.97; 95% CI, 1.12 to 3.48) during the follow-up (median, 3.4 years).[47] However, the treatment effect was not substantial, even though a large proportion of OSA subjects had active treatments including meaningful weight reduction (31% with weight loss of ≥10% body weight), CPAP therapy (58%) with fair adherence (at least 4 hours of nightly use for ≥5 nights a week), and upper airway surgery (15%). The increased rates of stroke and death despite OSA treatment can be explained by older age (compared to a previous study[125]), with correspondingly increased vascular risk, prolonged exposure to OSA prior to the treatment, a relatively shorter duration of intervention, and changes in treatment effectiveness (weight regained, reduced CPAP adherence, or loss of surgery effect).[47] The study was not designed a priori to investigate treatment effects. An increased risk of cardiovascular and non-cardiovascular death in the OSA group was also re-

ported from a longitudinal analysis of the Wisconsin Sleep Cohort and the Multi-Ethnic Study of Atherosclerosis cohort.[127,128]

Summarizing the observational findings, prospective studies largely support a causal relationship between OSA and stroke (Table 1). Recent systematic meta-analyses reported that OSA was significantly associated with incident stroke (OR, 2.24; 95% CI, 1.57 to 3.19) (relative risk [RR], 2.02; 95% CI, 1.40 to 2.10).[50,130] However a few important issues should be considered. First, the effects of well-established cardiovascular risk factors other than age, including hypertension, diabetes, atrial fibrillation, and smoking, were smaller than that of OSA, which was generally not significant.[47,49,125,126] Optimal modification or treatment of well-established vascular risk factors was likely to reduce their influences on the outcomes in the study participants.[126] Second, the observational findings are inherently limited by study design and lack of randomization. The baseline characteristics among groups may differ by undefined factors other than chance. The "healthy adherer" effect, describing a better outcome in subjects compliant with any given intervention due to their health-conscious behavior or lifestyle, might bias the results in favor of CPAP therapy.[131,132] Studies with randomized designs are required to provide a better understanding of the causal relationship between OSA and stroke, as well as the therapeutic efficacy of CPAP in the prevention of stroke.

Randomized clinical trials

Well-designed randomized clinical trials (RCTs) of CPAP therapy for primary prevention of clinical outcomes such as stroke, coronary heart disease, or atrial fibrillation are scarce.[133] In an RCT, feasibility and study design are critically influenced by the expected rate of the primary endpoint, the predicted efficacy (and precision in application) of therapy, and the estimated duration of intervention, all of which affect the sample size required for sufficient statistical power. To examine the effects of interventions on hard clinical endpoints (e.g., stroke in OSA) requires a larger sample size and longer period of observation than needed for trials with surrogate endpoints (e.g., blood pressure or inflammation in OSA). Therefore, to assess the effect of therapy (e.g., CPAP) on clinical outcomes, secondary prevention studies may be more feasible.[134,135]

Recently the results from two RCTs were reported, testing the long-term efficacy of CPAP therapy for the prevention of cardiovascular events in subjects with established cardiovascular disease (coronary heart disease or stroke) and OSA.[60,61] The Sleep Apnea Cardiovascular Endpoint (SAVE) trial was a multinational RCT including 2,717 non-sleepy subjects with moderate-to-severe OSA (AHI ≥15/hr, but not with severe hypoxemia [oxygen desaturation <80% for >10% of recording time]) and established stroke or cardiovascular disease, who were subsequently randomized either to usual care with CPAP therapy or to usual care alone, and were followed for a mean period of 3.7 years.[60] The study tested the hypothesis that additional CPAP therapy reduced the risk of future cardiovascular events (a composite of vascular mortality, myocardial infarction, stroke, or hospitalization for vascular events). During the follow-up, the CPAP therapy did not effectively lower the incidence of predefined events compared with the usual care (HR, 1.10; 95% CI, 0.91 to 1.32). In the CPAP group (n=1,346), the adherence was only 3.3 hours per night on average, and fair (≥4 hr/night) in less than half of the subjects (42%). During the run-in period of a week with sham CPAP that was introduced to maximize the treatment adherence of the study participants, the required threshold of minimal adherence was an average of 3 hours per night, equivalent to 50% adherence in those who sleep 6 hours daily. In the prespecified propensity-score-matched analysis to compare the group with fair CPAP adherence (n=561) with matched controls, the reduction in the composite endpoint was not significant (HR, 0.80; 95% CI, 0.60 to 1.07), but a lower risk of stroke was found (HR, 0.56; 95% CI, 0.32 to 1.00; *P*=0.05). Another RCT, the Randomized Intervention with CPAP in CAD and OSA (RICCADSA) trial, was performed in patients with coronary artery disease and concomitant non-sleepy OSA (n=244; AHI ≥15/hr).[61] During the follow-up (median, 56.9 months), the incidence of the primary composite endpoint (repeat revascularization, myocardial infarction, stroke, or cardiovascular mortality) was not different between the groups with and without CPAP therapy, but based on the per protocol analysis, the risk was significantly lower in the CPAP adherent group (nightly use ≥4 hours) than in the non-compliant group or the untreated group (HR, 0.29; 95% CI, 0.10 to 0.86).

Both the large (SAVE) and the small scale (RICCADSA) RCTs failed to demonstrate efficacy of CPAP therapy. Negative findings in such high-profile trials underscore the need for future trials, and are vital contributors to recognizing and addressing the key factors to be considered in the design of future studies.[136,137] Several important aspects should be discussed in this context. Both trials included only non-sleepy OSA for ethical reasons (the expected harm to sleepy subjects if included but untreated). Excessive daytime sleepiness is a marker of higher levels of inflammation, insulin resistance, and blood pressure, compared with non-sleepy OSA.[138-140] By excluding sleepy subjects, the study sample was limited to a potentially lower-risk group, thus reducing its statistical power. Preceding RCTs on non-sleepy OSA populations have demonstrated that CPAP therapy is not effective in reducing blood pressure and pre-

venting cardiovascular risk or events including incident hypertension, despite improvements in subjective sleepiness.[141-145] Therefore the lack of CPAP efficacy in trials performed with non-sleepy subjects cannot be generalized to severe or symptomatic OSA populations.

Another major issue is the therapeutic effectiveness of CPAP in these trials. CPAP adherence is a critical factor in therapeutic effectiveness. In the SAVE trial, the average nightly use was 3.3 hours, 20% of the subjects did not use CPAP at all, and only 42% used CPAP for at least 4 hours a night. The 4-hour threshold is an insurance-payment driven criterion widely enforced in the United States, which has gradually morphed into a clinical standard. The flaw in this sort of "criteria creep" is emphasized. Such a low adherence may have contributed to the null findings, as the residual apnea burden (see below) is substantial. Adherence to CPAP has modified efficacy in previous trials:[145-147] the higher the adherence, the better the outcome. A dose-response association between CPAP adherence and cardiovascular outcome was found in the SAVE and RICCADSA trials, in which CPAP adherence was related to a lower risk of stroke (HR, 0.56; 95% CI, 0.32 to 1.00) or cardiovascular endpoints (HR, 0.29; 95% CI, 0.10 to 0.86).[60,61] However these findings came from secondary or on-treatment analysis, possibly biased by multiple comparisons or a healthy adherer effect.[131,132] In addition to adherence, the timing and the duration of CPAP-off periods affect therapeutic effectiveness.[148-152] The CPAP-off time is likely to predominate in the latter half of the night, when REM sleep is prevalent. OSA events during REM sleep are generally prolonged and associated with severe oxygen desaturation. Sleep apnea during REM, but not during NREM sleep, has been associated with hypertension, non-dipping of nocturnal blood pressure, and insulin resistance, even in subjects not considered to have OSA (AHI <5/hr).[153-156] In recent observational finding from the Sleep Heart Health Study, severe REM OSA (AHI during REM sleep ≥30/hr) was associated with a higher incidence of cardiovascular events in the group with prevalent cardiovascular disease.[157] The cardiovascular effects of REM OSA have several important implications. The timing and duration of the CPAP-off periods as well as the subjects' sleep should be documented to define and interpret the effectiveness of intervention. The residual apnea burden, including REM OSA, is directly influenced by the proportion and timing of CPAP-on and -off periods.[148-150] In future trials, a predefined secondary analysis of REM OSA should be performed, considering its significant cardiovascular effects and prevalence.[158] REM OSA in subjects with AHI of <5/hr may bias the results of RCTs, especially secondary prevention trials.[157] From a diagnostic standpoint, simple cardiorespiratory monitoring devices, for example, a portable device consisting of airflow and oximetry, should not be used in future trials. Such a home kit cannot reliably detect REM OSA, central sleep apnea, and periodic limb movements (PLMs).[159] The latter two conditions are not only commonly present in high risk populations for cardiovascular events (such as the elderly or subjects with established cardiovascular diseases or stroke), but also increase the cardiovascular risk of these individuals.[160-164]

Finally, there is clear evidence that what is called OSA is a complex pathophysiological condition, with multiple and often interacting disease drivers.[165-167] These include upper airway collapsibility, impaired negative pressure response, reduced arousal threshold and high loop gain. The first three become irrelevant when the airway is adequately supported, but high loop gain will cause ongoing respiratory control instability and a high residual apnea burden or treatment intolerance. The risk of high loop gain is increased in those with cardiovascular comorbidities, setting the stage for impaired therapeutic responses.[166] Multi-modal therapy, such as low dose acetazolamide plus CPAP,[168,169] may reasonably be considered in future clinical trials. The quality of data, specifically direct visualization of respiratory waveforms from current generation CPAP devices, can also detect residual disease burden and help identify those who could benefit from multi-modal therapy.[170] The question should not be whether CPAP is beneficial, but whether effective sleep therapy is beneficial.

Previous RCTs on cardiovascular outcomes usually adopted composite endpoints, mainly due to considerations of feasibility and statistical power. However, for future trials, therapeutic efficacy needs to be tested separately for each type of cardiovascular endpoint. Stroke is a primary candidate for this purpose. In CPAP trials and observational studies, OSA was more strongly related to stroke than to other cardiovascular diseases. In the SAVE trial, CPAP adherence led to the reduced risk of stroke (HR, 0.56; 95% CI, 0.32 to 1.00), and untreated OSA in women was associated with an increased incidence of cardiovascular events, particularly stroke (HR for stroke, 6.44; 95% CI, 1.46 to 28.3; and HR for coronary heart disease, 1.77; 95% CI, 0.76 to 4.09), which is concordant with the findings of the Sleep Heart Health Study concerning the relationship between OSA and stroke occurrence.[49,60,171]

To summarize, we caution against discarding the benefit of CPAP therapy for the prevention of stroke and other cardiovascular events in OSA on the basis of results from the currently available RCTs. The overall findings suggest what really matters is the therapeutic effectiveness, which is determined by CPAP adherence, CPAP efficacy, apnea burden,[148-150] and possibly disease phenotype.[165-167] Apnea burden is driven by residual or

Table 2. Studies between sleep duration and risk of stroke or mortality

Study	Design	Number	Major findings*
Chen et al. (2008)[172]	Cohort 7.5 yr follow-up	93,175 women	≤6 hr of sleep : RR for ischemic stroke, 1.22 (1.03–1.44) 8 hr, 9 hr of sleep : RR for ischemic stroke, 1.14 (0.97–1.33), 1.24 (1.04–1.47)
Helbig et al. (2015)[173]	Cohort 14 yr (mean) follow-up	17,604	≤5 hr of sleep : HR for stroke, 1.44 (1.01–2.06) ≥10 hr of sleep : HR for stroke, 1.63 (1.16–2.29)
Kawachi et al. (2016)[181]	Cohort 17 yr follow-up	27,896	≥9 hr of sleep : HR for stroke mortality, 1.51 (1.16–1.97) : HR for ischemic stroke mortality, 1.65 (1.16–2.35)
Leng et al. (2015)[51]	Cohort 9.5 yr follow-up	9,692	≥8–9 hr of sleep : HR for stroke, 1.46 (1.08–1.98)
Pan et al. (2014)[178]	Cohort 14.7 yr follow-up	63,257	≤5 hr of sleep : HR for stroke mortality, 1.25 (1.05–1.50) ≥9 hr of sleep : HR for stroke mortality, 1.54 (1.28–1.85)
Qureshi et al. (1997)[182]	Cohort 10 yr follow-up	7,844	>8 hr of sleep : RR for stroke, 1.5 (1.1–2.0) >8 hr of sleep with daytime somnolence : RR for stroke, 1.9 (1.2–3.1)
von Ruesten et al. (2012)[174]	Cohort 7.8 yr (mean) follow-up	23,620	<6 hr of sleep : HR for stroke, 2.06 (1.18–3.59)
He et al. (2017)[52]	Meta-analysis 7.8–14.7 yr follow-up	528,653	RR for stroke (7 hr as reference) : 4 hr, 1.17 (0.99–1.38); 5 hr, 1.17 (1.00–1.37); 6 hr, 1.10 (1.00–1.21); 8 hr, 1.17 (1.07–1.28); 9 hr, 1.45 (1.23–1.70); 10 hr, 1.64 (1.4–1.92)
Li et al. (2016)[175]	Meta-analysis 3–18 yr follow-up	522,163	Short sleep duration (7 hr as reference) : RR for stroke, 1.07 (1.02–1.12) for each 1-hr shorter Long sleep duration (7 hr as reference) : RR for stroke, 1.17 (1.14–1.20) for each 1-hr increase : RR for stroke mortality, 1.17 (1.13–1.20) per 1-hr increase

RR, relative risk; HR, hazard ratio.
*Adjusted HR or RR (95% confidence interval).

emergent sleep apnea during CPAP-on and-off periods along with the duration of CPAP-off periods.[150-152,170] In future trials for primary and secondary prevention in OSA, we need to adopt methods to determine the therapeutic effectiveness by measuring apnea burden, and to test whether effective therapy (defined by minimal or sufficiently low apnea burden, e.g., measured average AHI <5 over the entire treatment period including both CPAP-on and -off state in sleep) reduces the risk of stroke and other cardiovascular events.

Sleep duration and insomnia

Sleep duration

The relationship between sleep duration and stroke incidence is U-shaped in general; the risk for stroke is elevated in both short and long sleep groups.[172-174] In a recent meta-analysis (n=559,252), the pooled HR for stroke was 1.15 (95% CI, 1.07 to 1.24) for short sleep and 1.45 (95% CI, 1.30 to 1.62) for long sleep duration.[51] In another study, the pooled RR for stroke was 1.07 (95% CI, 1.02 to 1.12) and 1.17 (95% CI, 1.14 to 1.20) for each 1-hour decrease and increase in sleep duration, respectively.[175]

Short sleep, commonly defined as <5 to 6 hours of nocturnal sleep, increases the risks of stroke, coronary heart disease, and death (Table 2).[52,173,175-180] In a large-scale prospective study of older women (Women's Health Initiative Study; age, 50 to 79 years; n=93,175), short sleep (≤6 hours) was associated with ischemic stroke (HR, 1.22; 95% CI, 1.03 to 1.44) in the group free from cardiovascular diseases and diabetes at the baseline.[172] Despite the large sample size, the study was limited by the participants' characteristics, as enrollment was restricted to postmenopausal women. In the European Prospective Investigation into Cancer and Nutrition-Potsdam Study (n=23,620; age, 35 to 65 years; men 38.6%), subjects with short sleep (<6 hours) had a significantly increased risk for stroke (HR, 2.06; 95% CI, 1.18 to 3.59) during the 8-year follow-up.[174] In anoth-

er population-based prospective study (n=17,604; age, 25 to 74 years; mean follow-up, 14 years), short sleep (≤5 hours) was significantly associated with stroke in men (HR, 1.44; 95% CI, 1.01 to 2.06).[173]

Long sleep duration (more than 9 hours of sleep) is also associated with stroke and cardiovascular mortality.[51,178,179,181,182] Qureshi et al.[182], using the First National Health and Nutrition Examination Survey (NHANES I), reported that stroke risk was higher in people who reported sleeping for >8 hours than for those who slept 6 to 8 hours (RR, 1.5; 95% CI, 1.1 to 2.1). In a recent population-based prospective study of 9,692 stroke-free participants, long sleep (HR, 1.46; 95% CI, 1.08 to 1.98), but not short sleep (HR, 1.18; 95% CI, 0.91 to 1.53), was associated with a higher risk of stroke.[51]

The association between sleep duration and stroke mortality has been assessed in several prospective studies[178,183] and meta-analyses.[52,175,184] The Singapore Chinese Health Study (n=63,257) showed that long (≥9 hours) and short (≤5 hours) sleep duration (compared with 7 hours of sleep) were significantly associated with increased risk for total stroke mortality (HR, 1.54; 95% CI, 1.28 to 1.85; and HR, 1.25; 95% CI, 1.05 to 1.50, respectively).[178] A meta-analysis showed that stroke mortality increased at either end of the sleep duration range.[184] However, other studies have found that the risk of stroke mortality increased only for long sleep duration, not for short sleep.[52,175,181,183]

When interpreting the relationship between sleep duration and the risk of stroke or mortality, a few issues need to be considered. First, in most epidemiologic studies the assessment of sleep duration was based on self-report, not on objective measurement. Although self-reported sleep duration generally correlates to a degree with the duration measured by actigraphy or polysomnography,[185,186] reported sleep duration is systematically over-estimated, especially in short sleepers, compared with objectively measured sleep duration.[187] Second, long sleep has a greater effect on mortality than short sleep,[52,181,188] which can be explained by differences in the driving forces for each end of the sleep spectrum. In contrast to short sleep, which commonly results from voluntary sleep curtailment due to social requirements or individual preferences, long sleep indicates an increased need for sleep, especially in the elderly, influenced by comorbid medical conditions such as chronic devastating illness or inflammation.[52,189-191] Short sleep is a modifiable behavioral risk factor with a small but significant impact on cardiovascular morbidity and mortality. Long sleep is an indicator of comorbid medical conditions that confer higher mortality and vascular risk. A longitudinal observational study of the Whitehall II Cohort demonstrated the differential effects of short and long sleep: a decrease in sleep duration was associated with increased cardiovascular mortality, while an increase was related to non-cardiovascular death.[192]

The linking mechanisms between short sleep and cardiovascular events include obesity, impaired glucose metabolism, hypertension, and dyslipidemia. Sleep loss contributes to the development of obesity or weight gain by disturbing the balance between energy intake and expenditure. Sleep deprivation leads to increased levels of the appetite stimulating hormone ghrelin and reduced levels of the anti-appetite hormone leptin.[193,194] Furthermore, reduced physical activity associated with sleep deprivation leads to weight gain by decreasing energy expenditure.[195,196] Short sleep is also associated with sympathetic overactivity,[197] which leads to impaired glucose metabolism,[180,198] hypertension, and non-dipping of blood pressure.[176,199,200] Sleep loss alters lipid metabolism.[177,201,202] Insufficient sleep activates inflammatory pathways, as indicated by increased levels of C-reactive protein and interleukin-6.[203,204]

Long sleep duration has been suggested as a potential marker for subsequent stroke risk.[51,52,175,181,182] The linking mechanisms between long sleep and stroke are still elusive, but increased inflammation and abnormal lipid profiles in long sleepers have recently been reported.[202,205] Long sleep has been associated with cardiovascular conditions including carotid artery atherosclerosis,[206] atrial fibrillation,[207,208] and white matter hyperintensities.[209]

In summary, both short and long sleep duration are associated with a higher risk for stroke and mortality. Each end of the sleep duration spectrum has different implications. Short sleep confers an increased risk for cardiovascular events and mortality, via effects on blood pressure, glucose and lipid metabolism.[52,175,210,211] Long sleep is often an epiphenomenon of comorbidities that are commonly associated with increased sleep fragmentation, depressive symptoms, and poor general health.[212] The effects of sleep duration can have substantial long-term consequences, considering the increasing longevity of humans. Interventions such as sleep extension in short sleepers might reduce the cardiovascular risks. Simple measures to cope with sleep debt such as napping or weekend sleep extension might have a meaningful impact at the population level. Recent studies found that weekend catch-up sleep was associated with a lower risk of hypertension and obesity.[213,214]

Insomnia

Insomnia is prevalent in approximately 10% to 20% of the adult population, with approximately 50% having a chronic form.[215] Chronic insomnia disorder is characterized by a complaint of difficulty initiating sleep and maintaining sleep, and

Table 3. Studies of insomnia, PLMS, RLS as a prognostic factor for stroke and mortality

Study	Design	Number	Major findings*
Insomnia			
Chien et al. (2010)[217]	Cohort 15.9 yr (median) follow-up	3,430	RR for CAD/stroke, 1.8 (1.0–3.1) RR for mortality, 1.7 (1.2–2.5)
Phillips et al. (2007)[219]	Cohort 6 yr follow-up	11,863	OR for hypertension, 1.2 (1.0–1.3) OR for CVD, 1.5 (1.1–2.0)
Vgontzas et al. (2009)[220]	Cross-sectional	1,741	<5 hr vs. >6 hr of sleep : HR for hypertension, 5.1 (2.2–11.8); OR for diabetes, 3.0 (1.2–7.0)
Wu et al. (2014)[53]	Cohort 4 yr follow-up	21,438	Insomniacs vs. non-insomniacs : adjusted HR for stroke, 1.54 (1.38–1.72)
PLMS			
Kendzerska et al. (2014)[225]	Retrospective 5.7 yr (median) follow-up	10,149	PLMI 13.4 vs. 0 : OR for stroke, 1.01 (0.94–1.09); OR for mortality, 1.05 (1.02–1.07)
Koo et al. (2011)[55]	Cohort 4.4 yr follow-up	2,911 men	PLMI >30 vs. <5 : OR for CVD, 1.25 (1.00–1.56)
RLS			
Elwood et al. (2006)[231]	Cohort 10 yr follow-up	1,874 men	OR for stroke, 1.67 (1.07–2.60)
Molnar et al. (2016)[232]	Cohort 8.1 yr follow-up	7,392	HR for stroke, 3.89 (3.07–4.94)
Szentkirályi et al. (2013)[233]	Cohort 6–11 yr follow-up	DHS: 1,312 SHIP: 4,308	OR for stroke DHS: 1.59 (0.17–15.16) SHIP: 1.20 (0.46–3.17)
Winkelman et al. (2008)[230]	Cross-sectional	3,433	OR for hypertension, 1.3 (0.9–1.8) OR for CAD/stroke, 2.4 (1.6–3.7)
Winter et al. (2013)[234]	Cohort 6 yr follow-up	48,938	OR for stroke (women), 1.29 (0.91–1.82) OR for CVD mortality (men), 1.22 (0.87–1.70)

PLMS, periodic limb movements during sleep; RLS, restless leg syndrome; RR, relative risk; CAD, coronary artery disease; CVD, cardiovascular disease; HR, hazard ratio; OR, odds ratio; PLM, periodic limb movement; PLMI, periodic limb movement index; DHS, Dortmund Health Study; SHIP, Study of Health in Pomerania.
*Adjusted RR, OR, or HR (95% confidence interval).

waking up earlier than desired. The diagnosis of chronic insomnia requires occurrences on at least three nights per week for at least 3 months.[216] Insomnia was found to be a risk factor for cardiovascular events and death in several studies.[190,217]

Sleep questionnaire-based studies have reported a significant association between insomnia symptoms and cardiovascular outcomes.[218] In a prospective study of 11,863 participants, subjective insomnia complaints were associated with an increased risk of hypertension and cardiovascular disease.[219] A large study of 21,438 subjects with insomnia and 64,314 matched controls found that the insomnia group had a 54% higher risk for stroke over a 4-year follow-up period than the control group.[53] However, these studies had the limitation that the diagnosis of insomnia was based solely on self-reported assessments or questionnaires for insomnia complaints, meaning that the sleep latency and time of being awake after sleep onset were generally overestimated.

Insomnia with objective short sleep duration (<5 hours on polysomnography), suggested as the most biologically vulnerable phenotype, carries a higher risk for impaired heart rate variability, hypertension, diabetes, neurocognitive impairment, and mortality, compared with insomnia with longer objective sleep (Table 3).[11,220-222] Insomnia with objective short sleep may show better response to biological treatments, whereas insomnia with objective normal sleep may show better responses to psychological interventions than to biological treatments.[11] Elevated sympathetic and hypothalamic-pituitary-adrenal axis activity has been proposed as a mechanism for the cardiovascular effect of insomnia.[11,220]

Periodic limb movements during sleep and restless legs syndrome

The defining feature of PLMS is periodic episodes of repetitive, highly stereotyped limb movements during sleep, which mostly occur in the lower extremities and can be associated with cor-

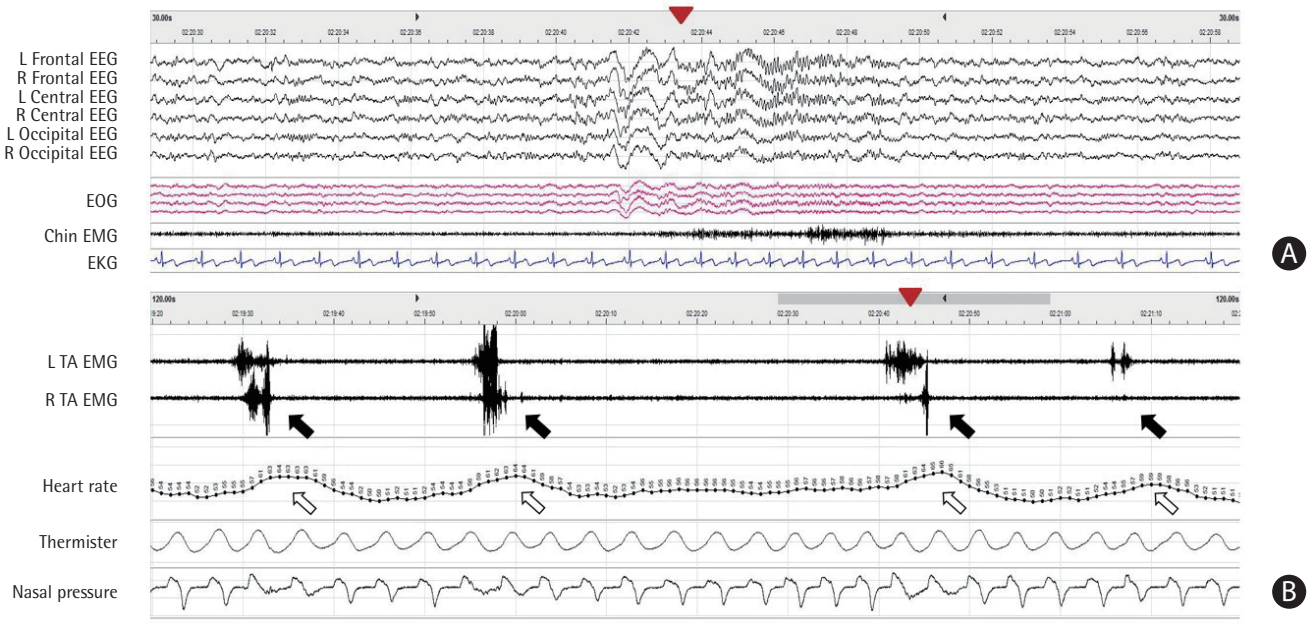

Figure 3. Periodic limb movements during sleep. (A) Electroencephalography (EEG) plots for 30-second epoch. Arousal (arrowhead in panel A) is accompanied by periodic limb movement (arrowhead in panel B) during stage 2 rapid-eye-movement (REM) and non-REM sleep. The closed arrowheads in panels A and B indicate the same time. (B) Movement event plots for 2-minute epoch. Heart rate surges (open arrows) are associated with periodic brief electromyography (EMG) bursts in left or right tibialis anterior (close arrows). L, left; R, right; EOG, electrooculography; EKG, electrocardiogram; TA, tibialis anterior.

tical arousal (Figure 3).[216] The presence and severity of PLMS is determined by the average number of PLMs per hour of sleep (PLM index). PLM is commonly present in the general population (4.3% to 9.3% with PLM index >15/hr) and even more commonly in restless legs syndrome (RLS) patients (80% to 88% with PLM index >5/hr).[223,224] PLM is not specific for RLS, as it is commonly seen with increasing age and in other medical disorders.[224] A positive relationship between PLM and cardiovascular events or mortality has been demonstrated in observational studies, and a greater risk attributed to PLM combined with arousals.[55,164,225,226] PLM with arousal induces an abrupt increase in blood pressure and heart rate through sympathetic overshoot.[227,228]

RLS is a chronic sensorimotor disorder characterized by an irresistible urge to move the limbs, which is usually worse at rest, occurs predominantly in the evening or night time, and is relieved by movement such as walking or stretching.[216,229] The prevalence of RLS in the general population has been reported to be between 5% and 10%, but it has been under-recognized.[164] RLS and its associated condition PLM may increase the risk for cardiovascular and cerebrovascular diseases.[230] Several studies showed that RLS might be a prognostic factor for stroke, although others obtained conflicting results (Table 3).[230-234] In a large prospective cohort study, RLS tended to be associated with an elevated risk of total and cardiovascular mortality, and this association between RLS and mortality increased in women with a longer duration of RLS diagnosis.[235,236] However, two meta-analyses assessing RLS as a risk factor for incident cardiovascular events and all-cause mortality were inconclusive.[163,164] More severe, longer duration exposures, and secondary forms of RLS were associated with increased risk for stroke.[164,230,237]

Sympathetic overactivity, metabolic dysregulation, inflammation, oxidative stress, peripheral hypoxia, and hypothalamic-pituitary-adrenal activation have been proposed as possible linking mechanisms between PLM/RLS and cardiovascular diseases.[238] Repeated nocturnal fluctuations in heart rate and blood pressure that are associated with PLM and related microarousals cause daytime hypertension, subsequently increasing the risk for cerebrovascular diseases.[227,228] In a prospective study of 3,116 elderly men, PLM increased atrial fibrillation risk in age-dependent manner.[239]

Circadian rhythm disorders and stroke

Circadian rhythms are endogenous biological rhythms with near-24-hour periodicity. The internal near-24-hour circadian pacemaker is entrained to the 24-hour light-dark cycle by exogenous cues (primarily light/dark cues, but also eating, and to lesser degrees exercise and social interactions).[216] Shift workers

are vulnerable to disruption of normal circadian rhythms. Shift work sleep disorder is characterized by complaints of excessive sleepiness or insomnia that occur when work hours overlap with the usual sleep time. Night shift work is associated with significant interference with the endogenous nocturnal blood pressure decline, resulting in abnormally elevated blood pressure during the shift that persists into the following day.[57] Shift workers are at risk for obesity, hypertension, diabetes, cardiovascular disease, and overall mortality.[240-243] In a cohort study of 80,108 nurses, rotating night shift work was associated with a 4% increased risk of ischemic stroke for every 5 years of exposure, after adjusting for standard vascular risk factors.[58] A recent systematic meta-analysis demonstrated that shift work was associated with ischemic stroke (RR, 1.05; 95% CI, 1.01 to 1.09), although the original studies showed mixed results.[244] Further studies should attempt to clarify the relationship between circadian rhythm disorders (including shift work sleep disorder) and stroke risk, as shift work is common and likely to increase.

Conclusions

Sleep disorders are highly prevalent in patients at risk for stroke, and may be modifiable risk factors for stroke. OSA increases the risk of stroke independently, but the reported lack of therapeutic effectiveness of CPAP for stroke prevention and cardiovascular protection should be cautiously interpreted. New clinical trials with improved therapeutic precision are necessary. Short or long sleep duration, and insomnia with objective short sleep duration, could be risk factors for stroke and mortality. Sleep-related movement disorders, including PLMS and RLS, are also potential risk factors for stroke. The overall findings suggest that systematic screening and proper management of sleep disturbances can substantially contribute to stroke risk modification at the population level.

Disclosure

Robert J. Thomas is co-inventor and patent holder of the ECG-derived sleep spectrogram, which may be used to phenotype sleep quality and central/complex sleep apnea. The technology is licensed by Beth Israel Deaconess Medical Center to MyCardio, LLC. He is also co-inventor and patent holder of the Positive Airway Pressure Gas Modulator, being developed for treatment of central/complex sleep apnea. He is a consultant in software development for DeVilbiss. The other authors have no financial conflicts of interest.

Implementation and feasibility of the stroke nursing guideline in the care of patients with stroke: a mixed methods study

Abstract

Background: Nurses often have difficulties with using interdisciplinary stroke guidelines for patients with stroke as they do not focus sufficiently on nursing. Therefore, the Stroke Nursing Guideline (SNG) was developed and implemented. The aim of this study was to determine the implementation and feasibility of the SNG in terms of changes in documentation and use of the guideline in the care of stroke patients on Neurological and Rehabilitation wards, barriers and facilitators, and nurses' and auxiliary nurses' view of the implementation.

Methods: A sequential explorative mixed method design was used including pre-test post-test measures and post intervention focus groups interviews. For the quantitative part retrospective electronic record data of nursing care was collected from 78 patients and prospective measures with Barriers and Facilitators Assessment Instrument (BFAI) and Quality Indicator Tool (QIT) from 33 nursing staff including nurses and auxiliary nurses. In the qualitative part focus groups interviews were conducted with nursing staff on usefulness of the SNG and experiences with implementation.

Results: Improved nursing documentation was found for 23 items ($N = 37$), which was significant for nine items focusing mobility ($p = 0.002$, $p = 0.024$, $p = 0.012$), pain ($p = 0.012$), patient teaching ($p = 0.001$, $p = 0.000$) and discharge planning ($p = 0.000$, $p = 0.002$, $p = 0.004$). Improved guideline use was found for 20 QIT-items ($N = 30$), with significant improvement on six items focusing on mobility ($p = 0.023$), depression ($p = 0.033$, $p = 0.025$, $p = 0.046$, $p = 0.046$), discharge planning ($p = 0.012$). Facilitating characteristics for change were significantly less for two of four BFAI-subscales, namely Innovation ($p = 0.019$) and Context ($p = 0.001$), whereas no change was found for Professional and Patient subscales. The findings of the focus group interviews showed the SNG to be useful, improving and providing consistency in care. The implementation process was found to be successful as essential components of nursing rehabilitation were defined and integrated into daily care.

Conclusion: Nursing staff found the SNG feasible and implementation successful. The SNG improved nursing care, with increased consistency and more rigorous functional exercises than before. The SNG provides nurses and auxiliary nurses with an important means for evidence based care for patients with stroke. Several challenges of implementing this complex nursing intervention surfaced which mandates ongoing attention.

Keywords: Stroke, Nursing, Evidence based care, Clinical practice guidelines, Feasibility studies

Background

Stroke generally results in life-altering changes for both patients and their closest family. Patients experience a whole arena of physical and psychosocial impairments [1]. In the long term 25–74% of patients have to rely on assistance of family for the help in basic Activities of Daily Living (ADL's) like feeding, self-care, and mobility due to the physical impairments, like paralysis of one side of the body, decrease in abilities such as reaching and handling objects [2]. Difficulties with posture and balance make it difficult for patients to walk and mobilize. About one-third of patients are confronted with cognitive impairments such as speaking and comprehending language [3] and many patients have difficulties with memory, which makes it difficult for patients to acquire and maintain new information [4]. Patients are confronted with the huge challenges due to changes in self-identity, role capacity and their abilities to properly function in their personal and social roles as a parent, partner or employee [5]. Stroke rehabilitation is a cyclic process which includes: assessing the needs of the patient, defining realistic and attainable goals, interventions or activities to achieve the goals and reassessment of the progress against the goals [6]. Rehabilitation is provided by an interdisciplinary team of health care professionals, including nurses, physical therapists, occupational therapists and other professionals, who support the patient to regain abilities that were lost. For the patient this is a time-intensive, effortful and often exasperating process [5, 7]. There is strong evidence that task-oriented training aiming to target functional tasks and ADL's can assist the natural recovery pattern of functional recovery [6]. Task-specific and context-specific training are well accepted evidence based principles in stroke rehabilitation as well as the principle that increased intensity of training facilitates recovery [6, 8, 9]. Goals for training need to be relevant for the patient and occur in the patient's environment, preferably his home surroundings. Generally, the literature emphasizes that patients with stroke need more rehabilitation training [8, 9].

Neuroscience nurses in stroke care are increasingly adapting to Evidence Based Practice integrating the best available evidence from well-designed studies with clinician's expertise and with information about patient preferences and values in making the best clinical decisions [10]. Although many Interdisciplinary Stroke Practice Guidelines have been developed for the rehabilitation and management of patients with stroke, these guidelines are often not routinely incorporated into daily nursing practice. Among the reason for this is the fact that these guidelines often lack information about early detection of problems using valid and reliable instruments and interventions relevant and feasible for nurses to use in the daily context of stroke care and are not routinely incorporated into the daily patient care [4, 11, 12]. In an attempt to provide information on various important areas in stroke care, nurses, patients and health care professionals in Iceland and the Netherlands collaborated in developing the Clinical Nursing Rehabilitation Stroke Guideline Stroke (CNRS-Guideline) [13]. Systematic reviews were conducted on interventions and instruments feasible for nurses to use in following areas: mobility and ADL [9], communication and aphasia [3], depression (in patients with/without aphasia) [14, 15], falls [16], neglect [17], self-efficacy [18]. A feasibility study provided evidence for the usability of this guideline for patients and nurses in Dutch stroke settings [19]. Continuing work is taking place and studies are conducted with nurses on identification of symptoms of depression in patients with stroke [20, 21] and aphasia [22, 23], neglect and how to develop and use technical applications in the rehabilitation of patients with stroke residing at home. Based on this work, the Stroke Nursing Guideline (SNG) was developed and adapted including recommendations targeting among other important elements like mobility and ADL, falls, depression, pain and education of patients and family [24].

Nurses, as key members of the rehabilitation team, provide nursing specific rehabilitation through the continuum of care [8, 9]. They train patients in activities of daily living, as training needs to be functional, task oriented as well as context specific [6, 8, 9]. As patients with stroke need more training, they play an essential role in creating more opportunities for patients to exercise and practice functional tasks outside and in-between formal therapy sessions [9]. Accordingly nurses need to maximize their contribution in activation of patients and integration of functional and task oriented training exercises in simple activities, targeting mobility and ADL in the context of daily nursing care in order to increase the intensity and duration of rehabilitation exercise and training.

Painful shoulder is a common, complex and distressing complication after stroke which interferes with patients' recovery. Many patients experience painful shoulder in the early stage of stroke, which continues into the chronic stage, with an incidence ranging from 12 to 58% [25]. Although various therapeutic treatments have been developed, outcome studies show contrasting findings [25, 26].

Depression is a frequent complication after stroke affecting up to one third of patients [27]. Depression after stroke negatively impacts patients' participation in rehabilitation, leads to worse functional outcome [28, 29] and higher mortality [30]. Although various guidelines recommend screening for depression in all stroke patients [4], depression after stroke remains unrecognized, undiagnosed and under treated [28]. Nurses routinely

screen patients for depression which increases the early recognition of depression [31] and they effectively identify depression after stroke using the Patient Health Questionnaire [20, 21, 32].

Falls are common among stroke patients with prevalence ranging from10 to 73% [16, 33, 34]. The various risk factors for falls reported include: instability when walking, weakness of the lower leg muscles, urinary incontinence, frequent need to go to the toilet, confusion, depression and medication [16], a Barthel Index score below 15, time since stroke longer than 12 weeks, first fall associated with visuospatial neglect [35] older age, increased length of stay [36], greater stroke severity, history of anxiety, history of fear of falling [37], lower functional status and lower cognitive status [38]. Although moderate evidence was found for the ability of instruments to predict risk of fall in patients after stroke, the literature recommends preventive screening for risk of falls and to provide preventive measures for risk of falls in all phases after stroke [16, 33–38].

Education is an important aspect in the care of patients and families during the stroke recovery [39]. Due to the complexity of the impairments and the huge changes in life after the stroke incident, patients and caregivers have diverse educational needs which often are not met [40]. Patients and caregivers reported that they need education about the clinical aspects of stroke, stroke prevention, treatment and functional recovery and caregivers also need information concerning moving and lifting patients, exercises, psychological changes and nutritional issues after stroke, that is tailored to their situation [40]. Lack of knowledge about stroke can lead to misconceptions, anxiety, fear, poor health status and emotional problems [39, 40]. Therefore patients and caregivers need more and thorough education, tailored to their needs, after the stroke.

The Medical Research Council emphasizes the importance of evaluating feasibility and implementation of complex interventions like guidelines, in terms of acceptance by health care professionals, the nursing staff knowledge and skills and the facilities needed for implementation [41, 42]. Feasibility is referred to as the quality of being useful and practical and involves study of the applicability or practicality, which can be assessed by considering the acceptability of the guideline to clients and staff administering it, the costs and the ease of integrating it into clinical settings [43]. Implementation is defined as the introduction of an innovation in daily routines, demanding effective communication, and removing obstacles [12]. Unfortunately, the literature shows that implementation of CPGs is often not achieved and not following the evidence-based CPGs leads to suboptimal care for many patients [12]. Despite the evidence found for the usability of the earlier CNRS guideline, the fact that it was extensive and included many recommendations was found difficult for implementation [19].

Based on this background the aim of this study was to investigate the implementation and feasibility of the use of a Stroke Nursing Guideline (SNG) focusing on mobility ADL, depression, pain, falls, education and discharge planning, used by nurses and auxiliary nurses in the daily care of patients with stroke and stating the following research questions: a) What is the difference in nursing staff documentation of the screening and application of interventions for activities of daily living, mobility, depression, pain, falls, patient education and discharge planning of patients who receive rehabilitation nursing care before and after implementing the SNG? b) What are the nurses' and auxiliary nurses' view on the acceptability of using the SNG in supporting the provision of daily nursing care? c) What are the nurses' and auxiliary nurses' views on barriers and facilitators to implementing and embedding the SNG within routine daily nursing care?

Methods

This study used a sequential explorative mixed method design [44], including pre-test post-test measures [45] and focus group interviews [44]. The pre-test post-test was chosen to measure the difference in nursing staff documentation of the screening and application of interventions, whereas the focus group interviews explored the nurses' and auxiliary nurses' views of implementing and using the SNG. The study was conducted in three phases: In phase one (February 2012 to February 2013) pre-test retrospective patient record data were collected from: a) *patients'* electronic nursing documentation system (ENDS-system) on screening and application of key interventions in stroke care which included items focusing on: activities of daily living, falls, pain, depression, patient education and discharge planning, and b) *registered nurses* and *auxiliary nurses* answers on the Barriers and Facilitators Assessment Instrument (BFAI) [46] and the Quality Indicators Tool (QIT) reflecting the SNG. In phase two (April 2013 to the end of December 2013) the SNG was implemented using evidence based strategies including education and training, opinion leaders, posters and reminders [47, 48]. In phase three (February 2014 to February 2015), the posttest measurements were conducted with nurses and auxiliary nurses and patients assigned to the intervention group (February 2014 to February 2015). The focus group interviews were conducted with a subgroup of nurses and auxiliary nurses in October and November 2014 (Fig. 1). Hereafter, nurses and auxiliary nurses are generally referred to as nursing staff. To provide thorough reporting of the study both STROBE and COREQ statements were used (Additional file 1).

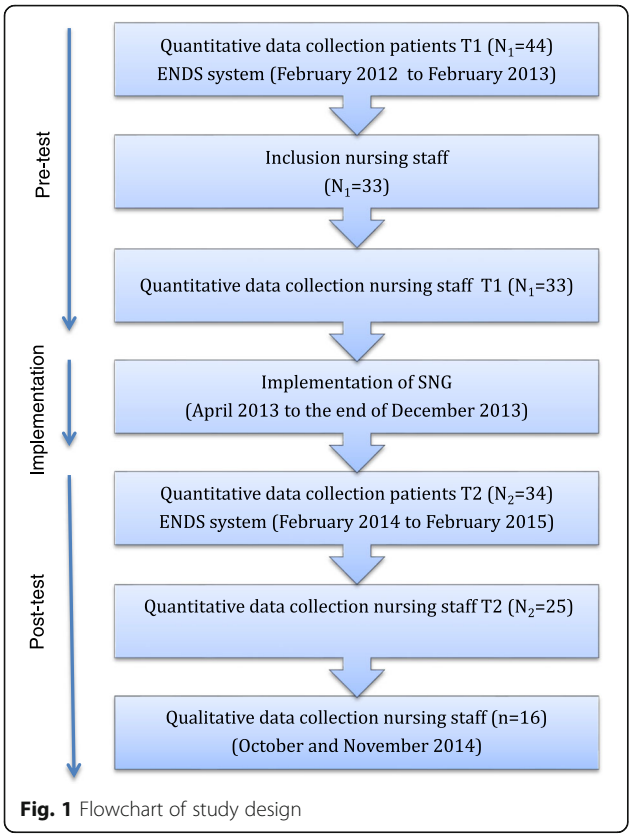

Fig. 1 Flowchart of study design

Setting and participants

The study was conducted at neurology and rehabilitation wards of a university hospital in Iceland. Patient records were extracted from all patients diagnosed with stroke, older than 18 years of age, admitted to the acute neurological ward and subsequently transferred to the rehabilitation ward for 12 months prior to implementation and for12 months after implementation. Excluded were patients who died while admitted to the wards. Data were retrieved from 78 patients (34 in the pretest and 44 in the posttest).

All nursing staff, which included registered nurses and auxiliary nurses working on the participating wards (N = 40, nurses = 22 and auxiliary nurses = 18), were invited to take part in the study and signed informed consent. Thirty-three nursing staff responded to the pre-test questionnaires, whereas 25 responded to the post-test questionnaires (18 nurses/15 nursing auxiliaries/pretest and 13 nurses/12 nursing auxiliaries/posttest). Sixteen nurses and auxiliary nurses (N = 8 each group, respectively) took part in three focus group interviews.

The stroke nursing guideline

The Stroke Nursing Guideline (SNG) aims to provide an overview of evidence based recommendations for the daily nursing care and rehabilitation of patients with stroke. The SNG was developed based on systematic reviews and studies focusing on following areas: mobility and ADL [8, 9], falls [16, 33–38, 49, 50], pain [25], depressive symptoms [14, 15, 20, 21, 28–32], education [39, 40, 51], as well as the CNRS-Guideline [13]. The authors, who all have extensive experience in stroke care and research, made the first selection of important interventions based on the literature, which were formulated as recommendations for the SNG.

Among important aspect of implementation and acceptability of new guidelines like the SNG is the fact that all professionals involved in the care of patients with stroke agree and support the guideline. Therefore, we approached a group of 20 interdisciplinary professional experts, to critically review the content, readability, layout and usability of the guideline. These experts included: nine nurses and of these seven worked on the wards, all with BSc degree in nursing and long experience in neuroscience nursing, of these four had a MSc degree and two had a PhD degree; six physical therapists, two occupational therapists; one psychologist; one rehabilitation physician and one neurologist. These professionals all agreed on the content of the guideline recommendations and their comments mainly focused on the readability, layout and usability of the SNG. There were no specific differences between the professionals in their views about the SNG and based on the expert feedback, the guideline was adapted and optimized.

The final SNG included a total of 23 recommendations focusing on assessment and therapeutic interventions categorized in the following areas: 1) activities of daily living and mobility and falls (14 recommendations), 2) pain/shoulder pain (3 recommendations); 3) depression (3 recommendations); 4) patient education (2 recommendations) and 5) discharge planning (1 recommendation). The guideline also included thorough instructions with photos on how to use the recommendations, with chapters on: background information, definition of concepts, flow-scheme of how to use the guideline, recommendations for the assessment of various outcomes including: mobility and activities of daily living using, the Functional Independence Measure (FIM) [52]; risk of falls using the Morse Fall Scale (MFS) [49]; shoulder pain using a visual analogue scale; depressive symptoms with Patient Health Questionnaire-9 (PHQ-9) [53, 54] and recommendations focusing on therapeutic interventions for the aforementioned areas as well as appendices with the instruments and instructions with photos on how to assist patients with mobility, exercises and positioning. The SNG guideline was made ready to use in a digital, online form as well as a 32 page manual including a plasticized card (pocket size) which was available for all staff.

Data collection

Patient data were retrieved from the ENDS-system including: demographic and health care data: age, sex, living situation, height, weight, health history, the clinical diagnosis of stroke and the type of stroke (provided by a neurologist, based on a CT-scan or an MRI). Also, the following data concerning 37 items on screening and application of key interventions in stroke care were retrieved from the ENDS-system:

a) *activities of daily living and mobility* (8 items) screened with the Functional Independence Measure (FIM) [52] within 72 h of admission, including diagnosis of mobility and ADL, evaluation of care, limitation in self-care, mobilization facilitation within 24 h, frequency of training exercises, walking exercises, training of ADL activities.
b) *fall and fall risk* (1 item) screened within 72 h using the Morse Fall Scale (MFS) [49], consisting of six items reflecting risk factors of falling: (i) history of falling, (ii) secondary diagnosis, (iii) ambulatory aids, (iv) intravenous therapy, (v) type of gait and (vi) mental status. Total score ranges between 0 and 125 [49]. MFS had been translated into Icelandic (MFS-I) and piloted with the nurses to determine their understanding of wording of items. Interrater reliability was examined and the level of agreement was 84% ($K = 0.68$) [49].
c) *pain assessment and pain treatment with special focus on shoulder pain* (14 items): Patients were asked about pain/shoulder pain and pain assessment was conducted using a visual analogue scale and the following interventions were provided: pain treatment (warm cold packages, massage), pain medication given, non-pharmacological treatment given, comforting, massage, relaxation, distraction, pain treatment never given, evaluation of pharmacological pain treatment).
d) *patient screening for depressive symptoms* (4 items): Patients were asked about psychological distress, nursing diagnosis of depression, consultation of other professionals for the diagnosis and treatment. Depression was screened with the Patient Health Questionnaire-9 (PHQ-9). The scores are summed to produce a value ranging from 0 (no depression) to 27 (all symptoms occurring nearly every day [53, 54]. Symptoms of depression with the PHQ-9 was only screened in the posttest because no depression scale existed in the electronic documentation system prior to the implementation.
e) *patient (and family) received education* (4 items) including standard information about stroke and rehabilitation, education brochure received, education repeated and tailored to the patient's (and family) needs.
f) *discharge planning* (6 items) which included: basic discharge planning using electronic patient record, quality discharge planning, patient discharge interview, social support recommended/planned, aftercare recommended/planned, written recommendations.

Demographic data of the nurses and auxiliary nurses were collected including: age, gender, education, experience/length of time working in stroke rehabilitation (0–2 years, 3–10 years, >10 years), current function (full time equivalent), courses on nursing stroke rehabilitation.

Barriers and facilitators for implementation were measured with the Barriers and Facilitators Assessment Instrument (BFAI) [46], with 27 questions, addressing four domains: *characteristics of the innovation* i.e. *the guideline; characteristics of the care provider, patient characteristics and context (organizational, social, political factors)*. The questions are positively as well as negatively formulated on a five-point Likert scale, ranging from 5 (strongly agree) to 1 (strongly disagree). The BFAI is a standardized and reliable instrument, with an item response of >90%, with each item having a distinctive character and was found to be useful for evaluating barriers and facilitators and with Cronbach's alpha for the four domains ranging from 0.63 to 0.68 [46].

The use of the guideline was measured with a Qualitative Indicator Tool (QIT), developed by the authors, based on the SNG recommendations as and included 30 statements, for the nurses. The QIT statements focused on the main areas of the SNG: a) mobility and activities of daily living (7), b) falls (1), c) depression (9), d) pain/shoulder pain (5), e) patient education (5) and f) discharge planning (3) and inquired if the nurses provided care according to the SNG-recommendations and were phrased in line with the following statement as an example: "I conduct assessment of mobility and self-care activities on admission with a) the FIM-scale, b) the scale in the electronic patient health records, c) both FIM scale and the scale in the electronic patient health records", which were scored on a five point Likert scale (almost never or <10% to very often or >90%). The face validity of the QIT was evaluated by a group of five experts and included clinical nurse specialists and nurse researchers with extensive experience in stroke nursing and rehabilitation, who reviewed the statements and concluded that the 30 statements were relevant for the daily care and rehabilitation of patients with stroke. Further psychometric testing of the QIT needs to be conducted.

Focus group interviews

Three Focus Group Interviews were conducted with eight nurses and eight auxiliary nurses after the implementation [44]. The interviews were chaired and conducted by a

clinical nurse specialist in geriatric nursing, who is a seasoned researcher and has experience with focus group discussion, but was not involved in this study in other ways. An assistant observed and took notes on the interviews, how participants responded to questions and how the discussion evolved. The project manager (IB) invited participants to the interviews but did not take part in them. In the first interview seven nurses ($N = 2$) and nurse auxiliaries ($N = 5$) took part, in the second interview four nurses ($N = 4$) and no auxiliary nurses took part, whereas in the third interview five nurses (N = 2) and nurse auxiliaries ($N = 3$) took part. An interview guide was used to guide the interviews. The findings of the previous interviews were used to guide discussion in the subsequent interviews (Additional file 2).

Procedure

Phase 1. Pre-test

Quantitative data of the pre-test group of patients were collected from the Ends-system prior to the implementation of the SNG. Pre-test measures of the nurses and auxiliary nurses were collected as well, after presenting the study including the purpose and procedures in a meeting with the nurses, nurse auxiliaries and managers of the ward.

Phase 2. Implementation

The SNG was implemented in the course of nine months using the following implementation strategies which were based on the literature [47, 48]: a) *Stroke Nursing Guideline:* all the registered nurses and auxiliary nurses received both a printed and plasticised version as well as a digital version. b) *Education and Training sessions:* All the registered nurses and auxiliary nurses as well as other professionals were invited to take part in one of two, four hour education and training session in how to use the recommendations, the screenings instruments and interventions recommended. This training was strongly recommended for the nurses and the nurse auxiliaries. c) *Opinion leaders*: seven nurses (5 registered nurses and 2 auxiliary nurses) took on the role of an opinion leader. The opinion leaders were experts in the content and application of the guideline. They followed up on the implementation of the guideline, observed if recommendations were used and gave advice to other colleagues concerning the application of the recommendations. d) *Posters and reminders:* Posters and reminders were placed on the walls of the wards to remind the nurses on using the guideline and e) E-mails: Regular e-mails were sent to all the registered nurses and auxiliary nurses explaining the intervention protocol and the recommendations.

Phase 3. Post-test

After the implementation period, the post-test data collection took place. The same data were collected as in the pre-test. In addition, focus group interviews were conducted with a subgroup of nurses and auxiliary nurses. The focus group interviews took place in a quiet room within the nursing science department and not within the hospital wards.

Data analysis

Quantitative data were analyzed using descriptive statistics to describe the characteristics of the patients including means (SD), medians (IQR) or n (%). Frequencies and percentages were reported for the recommendations used, perceived barrier quality indicators were analyzed and reported for both control and comparison group. Associations were calculated for specific patients' health problems and specific recommendations using Fisher's exact Test (2-sided) and Spearman's rho. All data were assessed for normality, which was taken into account when choosing the appropriated statistical method used. For analyzing the Perceived barriers and facilitators measured with the BFAI, the items 4–15 and 17–27 were revised so that a higher score reflected positive and low score negative view of participants. A p-value of <0.05 was considered significant. The SPSS version 20 (SPSS inc., Chicago IL, USA) was used.

Qualitative data analysis was carried out with content analysis (44). The first stage in the qualitative analysis process involved transcription of the interviews. The transcripts were studied repeatedly by two researchers (IB/HJ). Following the transcription, the content was checked for accuracy, after which the data were analyzed. The first level of analysis involved grouping that under broad headings in the interview guide and data were categorized to answer the research question(s) by extracting the quotes from the transcribed interviews. The authors read and reread the transcribed interviews, initial themes were identified using open coding of the data. Differences in themes were resolved by discussions (IB/HJ/TBH). Member checking was employed to ensure content validity by obtaining agreement from participating nurses on a summary of the focus group findings.

Quantitative and qualitative results were integrated after data analysis [44], results of these data were presented separately but integrated in the discussion section.

Research ethics

The study was conducted in accordance with the Declaration of Helsinki (revised form, Seoul 2013) [55]. The Hospital Ethics Committee (1909201223–2012, 0411201323–2012, 1,701,201,423–2012,1,603,201,523–2012, 1,007,201,523–2012, 23/2012), the Ethics Committee of the CEO of Medicine (3,005,201,516, 16LSH-14,1,203,201,516), Human

Resource Council of the hospital (2505201216) and the Data protection Authorities (2,012,050,710, 2,014,010,073, S6717–2014) approved the study. All the nurses and nursing auxiliaries consented to participation and the use of direct quotes in this paper by signing an informed consent form.

Results

Patients and nurses characteristics

In total data were extracted from 78 patients. Analysis was based on data from 44 patients in the pre-test group (T1) and 34 patients in the post-test group (T2) and Patients in both groups were comparable on main demographic variables, except that the patients in the post-test group were younger ($p = 0.051$) (Table 1). A total of 33 nursing staff were included in the study and of these 18 were registered nurses (54%) and 15 were nursing auxiliaries (46%). Of the group 25 (76%) worked on the rehabilitation ward whereas eight (24%) worked on the neurological ward. Most of the staff worked part-time (Table 2).

Table 1 Characteristics of patients

	Pre-test ($N = 44$)	Post-test ($N = 34$)	*p*-value
	Group	Group	
Gender (n,%)			0.246
Men	29 (66)	18 (53)	
Women	15 (34)	16 (47)	
Age (M, SD)	65.5 (13.12)	58.2 (17.90)	0.051
Disease diagnosis (n,%)			
Hemorrhage	11 (25)	8 (24)	0.881
Infarct	33 (75)	26 (76)	
Living situation (n,%)			0.763
Single/lives alone	11 (25)	10 (30)	
Married/cohabiting	32 (75)	23 (70)	
Employment status prior to admission[a](n,%)			0.438
Full employment	12 (29)	10 (35)	
Part time	2 (5)	1 (3)	
Not working	2 (5)	1 (3)	
Retired	20 (49)	9 (31)	
Disability benefits	5 (12)	8 (28)	
Nationality (n,%)			
Icelandic	44 (100)	31 (91)	0.044
Non-Icelandic	0 (0)	3 (9)	
Length of hospital stay days (M, SD)			
Neurological ward	17.8 (13.10)[b]	14.7 (7.162)	0.225
Rehabilitation ward	58.0 (48.27)	58.8 (56.71)	0.135

[a]Missing data, [b]2 patients excluded due to unusual long acute phase

Difference in documentation of SNG key interventions before and after implementation

Documentation of the 37 items on screening and application of key interventions in stroke care, was improved in 23 items after implementation. Significant improvement was found on the six following items: a) three items in ADL and mobility: Assess with FIM < 72 h of admission ($p = 0.002$), Mobilization facilitation within 24 h ($p = 0.024$), Training of ADL ($p = 0.022$) and b) three items on patient education: Patient education ($p = 0.001$), Educational brochure provided ($p = 0.000$) and Education repeated ($p = 0.049$). No change was found in the documentation of five items (4 pain variables, 1 depression). Significant worse documentation was found for the item Patients asked about pain ($p = 0.012$), whereas the worse documentation on the remaining eight items was non-significant (3 ADL, 4 pain, 1 depression) (Table 3).

Difference in the use of the SNG measured with the quality indicator tool

The nurses' use of the guideline measured with the 30 item QIT, showed enhanced use on 20 indicators, six of which the improvement was significant (Table 4). Improvement in use of the guideline was shown in seven indicators (of eight) on *Mobility and ADL*, with significant improvement in one item, namely *Assist and supervise patient with exercises according to physical therapists recommendations (p = 0.023)*. Improvement was shown in four (of eight) indicators on *Depression*, with significant improvement for three items: *Assess symptoms of depression with a depression scale (p = 0.033), Take time to talk with patient (p = 0.046), Take time to talk with family (p = 0.046)*. Non-significant improvement trend was shown in four (of five) indicators on *pain* as well as on two (of five) indicators on *Patient education* indicators. Improvement was shown on two (of four) indicators on *Discharge planning* and of these significant improvement was found for the indicator *Document discharge planning in patient electronic health records*. On the remaining 10 indicators no improvement was found (Table 4).

In the analysis of the focus group interviews the following six themes emerged: *Improved quality of care, Content known to staff, Convenient and concise, More use of instruments, More consistency, Illustrative and instructive.* The focus group interviews showed that the nurses and auxiliary nurses viewed the use of the guideline to improve nursing care. They knew the content of the guideline, used it and found the guideline practical and easy to use. The use of the SNG made them focus more

Table 2 Characteristics of nurses and auxiliary nurses ($N = 33$)[a]

	N (%)
Ward (n, %)	
Rehabilitation	25 (76)
Neurological	8 (24)
Profession (n, %)	
Registered nurses	18 (54)
Auxiliary nurses	15 (46)
Age (years) (n, %)	
< 34	10 (30)
35–44	3 (10)
45–54	5 (15)
55–64	10 (30)
> 65	5 (15)
Highest educational degree/diploma (n, %)	
Nursing Bachelor of Science/Diploma	14 (43)
Postgraduate nursing program	5 (15)
Nursing auxiliary program	12 (36)
Postgraduate nursing auxiliary program	2 (6)
Full time equivalent work (FTE) (n, %)	
100%	5 (16)
50–90%	24 (77)
40–49%	2 (7)
Working experience in nursing (years) (n, %)	
< 4 years	1 (3)
1–5	7 (21)
≥6	25 (76)
Working experience in stroke rehabilitation (years) (n, %)	
0–2	6 (19)
3–10	13 (42)
>10	12 (3)
Nursing stroke rehabilitation courses attended (n, %)	
Mobility/self-care	19 (58)
Psychological care	13 (39)
Patient education	12 (36)
Falls	12 (36)
Pain	15 (45)
Other	2 (6)

[a]There is lack of responses on all items, varying between 2 and 4

on specific issues like depression and falls and provided accurate and systematic way to evaluate and communicate about patients' progress. It provided consistency in care as they provided care and exercises in the same way, with consistency in intensity, frequency, with more rigorousness and better use of ergonomics than before. They found the guideline layout, including photos and diagrams, to be illustrative and instructive for patients, who are mobilized and cared for in a convenient and consistent way. Family members were more trustful in that the patients received optimal care. At the end of the focus group interview, the nurses and auxiliary nurses participating were individually asked to rate their view of the general usefulness of the SNG on visual analogue scale (ranging from 1 indicating not useful to 10 indicating very useful) which was valued with a mean score of 7.7 (range 5.5–9.0)(Table 5).

Nursing staff view of the implementation process

Facilitating characteristics for change were significantly less for two of the four subscales, namely Innovation ($p = 0.019$) and Context ($p = 0.001$) on the BFAI, whereas no change was found for Professional and Patient subscales (Table 6). Contrary to these results, the nurses and auxiliary nurses reported positive experiences, when asked to rate the success of implementation on visual analogue scale (ranging from 1 indicating not successful to 10 indicating very successful) which was valued as successful with a mean score of 7.5 (range 6.0–8.5). They maintained that the implementation brought a totally different view on mobilization in daily care (Table 5). In the analysis of the focus group data, the following six themes emerged: *Nursing rehabilitation defined and integrated, Physical exercise Individualized, Enhanced patient and family teaching, Coherent and consistent leadership, Improved staff education* and *Less visible nursing care received attention.* The focus group interviews showed that the nurses and auxiliary nurses found that throughout the implementation consistent and coherent leadership was provided. They found that essential components of rehabilitation had been defined and integrated into daily nursing care (standing up and sitting down, going to the toilet). The exercise guidelines made individual instructions from other professionals less needed. There was enhanced patient and family teaching, good teaching material, and consistent and good staff education. Previous less visible aspects of nursing care, after implementation, received attention and recognition among all staff. Of particular significance was the contribution this makes to the entire rehabilitation of patients with stroke (Table 5).

Discussion

This study investigated the implementation and feasibility of a newly developed Stroke Nursing Guideline using electronic data on patient outcomes before and after implementation and data from nursing staff on barriers and facilitators for implementation, quality indicators before and after implementation of the SNG and the views and opinions of nursing staff towards the guideline. In this way we aimed to gain better understanding of the implementation, use and feasibility of the SNG in daily

Table 3 Comparison of documentation of Quality Indicator Tool items of the Stroke Nursing Guideline

	Pre-test Group (N = 44)		Post-test Group (N = 34)		*p*-value[a]
	No (%)[b]	Yes (%)	No (%)	Yes (%)	
Mobility and Activities of daily living (n, %)					
Assess. with FIM < 72 h of admission	33 (75)	11 (25)	14 (41)	20 (59)	*0.002*
Nursing diagnosis of mobility	4 (9)	39 (91)	1 (3)	33 (97)	0.261
Evaluation of care	33 (75)	11 (25)	28 (85)	5 (15)	0.292
Limitation in self-care	17 (39)	27 (61)	9 (26)	25 (74)	0.258
Mobilization facilitation <24 h	19 (47)	21 (53)	7 (22)	25 (78)	*0.024*
Frequency of training exercises	12 (35)	22 (65)	10 (39)	16 (61)	0.180
Walking exercises	4 (14)	25 (86)	4 (17)	20(83)	0.778
Training of ADL activities	12 (30)	28 (70)	2 (7)	26 (93)	*0.022*
Falls (n, %)					
MORSE screening	34 (77)	10 (23)	21 (62)	13 (38)	0.306
Pain and pain treatment (n, %)					
Patients asked about pain	10 (23)	34 (77)	17 (50)	17 (50)	*0.012*
Pain diagnosis	10 (23)	34 (77)	6 (18)	28 (82)	0.582
Pain assessment with a scale	23 (74)	8 (26)	16 (73)	6 (27)	0.905
Fixed pain treatment	7 (21)	26 (79)	9 (39)	14 (61)	0.144
PN pain treatment	10 (30)	23 (70)	8 (32)	17 (68)	0.890
Non-pharmacological pain treatment	22 (73)	8 (27)	12 (55)	10 (45)	0.159
Comforting	42 (96)	2 (4)	32 (94)	2 (6)	0.589
Massage	43 (98)	1 (2)	31 (91)	3 (9)	0.217
Electrotherapy	44 (100)	0 (0)	34 (100)	0 (0)	–
Ankle splint	43 (98)	1 (2)	34 (100)	0 (0)	0.564
Relaxation	44 (100)	0 (0)	34 (100)	0 (0)	–
Distraction	44 (100)	0 (0)	34 (100)	0 (0)	–
Pain treatment never given	28 (78)	8 (22)	21 (78)	6 (22)	1.000
Evaluation of pain treatment	4 (14)	25 (86)	7 (33)	14 (67)	0.097
Depressive symptoms (n, %)					
Psychological distress diagnosis	18 (41)	26 (59)	15 (45)	18 (55)	0.690
Assessment with PHQ9	–	–	29 (88)	4 (12)	–
Identification of depressive symptoms	–	3 (7)	–	3 (9)	–
Consultation other professionals for the diagnosis and treatment	25 (58)	18 (42)	13 (38)	21 (62)	0.083
Patient teaching (n, %)					
Patient education	37 (84)	7 (16)	15 (47)	17 (53)	*0.001*
Educational brochure	40 (95)	2 (5)	15 (48)	16 (52)	*0.000*
Education repeated	30 (91)	3 (9)	30 (91)	14 (19)	*0.049*
Participation in teaching sessions	39 (89)	5 (11)	27 (82)	6 (18)	0.397
Discharge planning (n, %)					
Electronic Patient Record	11 (32)	23 (68)	18 (42)	25 (58)	0.393
Quality Discharge Planning*	7 (30)	16 (70)	22 (85)	4 (15)	*0.001*
Discharge Interview	22 (69)	10 (31)	43 (100)	0 (0)	*0.000*
Social support	7 (22)	25 (78)	14 (38)	23 (62)	0.151
Advice follow-up	20 (63)	12 (37)	36 (92)	3 (8)	*0.002*
Written infomation & recommendation	25 (81)	6 (19)	42 (100)	0 (0)	*0.004*

a) p-value calculated with Chi square test; p-value cursive indicates significant difference between groups;
b) No = very limited information documented; Yes = somewhat good and very good, with relevant information

Table 4 Difference in nurses' application of 30 quality indicators before and after implementation of the Stroke Nursing Guideline ($N = 14$)

	Pre-test group M (SD)	Post-test group M (SD)	*p*-value
Mobility and activities of daily living			
Assess mobility and self-care capabilities on admission to the ward with			
a) FIM scale	1.818 (0.982)	1.727 (0.273)	0.655
b) scale in patient electronic health records	2.909 (1.640)	3.091[a] (1.446)	0.672
c) both FIM scale and scale in electronic patient health records	1.750 (1.036)	2.000[a] (1.195)	0.157
Assist patient with getting in and out of the bed on the first shift on the ward	4.077 (0.760)	4.231[a] (0.726)	0.157
Assist and supervise patient to transfer between bed and chair	4.462 (0.877)	4.615[a] (0.650)	0.157
Assist and supervise patient with exercises according to physical therapists' recommendations	3.692 ((1.032)	4.308[b] (0.947)	*0.023*[b]
Assist patient in ADL and coach transferral of exercises into ADL	4.308 (1.109)	4.385[a] (0.768)	0.739
Assist patient with hemiplegia to exercise the paralysed arm	3.462 (1.050)	3.615[a] (1.193)	0.564
Assist patient with hemiplegia to make personal goals in writing if needed	3.846 (1.068)	3.769 (1.166)	0.705
Falls			
Assess risk of falls with MORSE scale	2.846 (1.519)	3.231[a] (1.092)	0.129
Pain			
Prevent shoulder pain by comforting the paralysed arm	4.846 (0.376)	4.923[a] (0.277)	0.317
Teach patient how to prevent shoulder pain	4.000 (1.000)	4.308[a] (1.109)	0.234
Teach family how to prevent shoulder pain	3.417 (0.669)	3.667[a] (0.888)	0.317
Grade patient's pain by pain scale	3.692 (1.109)	3.385 (0.961)	0.157
Use non-pharmacological pain interventions	3.250 (1.056)	3.833[a] (0.835)	0.107
Depression			
Assess symptoms of depression with a depression scale	1.231 (0.599)	1.846[b] (0.801)	*0.033*[b]
Refer patient to a psychologist due to depression	2.857 (1.351)	3.071[b] (1.207)	0.438
Refer patient to other HCPs e.g., chaplain or social worker	2.750 (1.139)	2.500 (0.798)	0.180
Provide emotional support e.g., with active listening	4.429 (0.646)	4.214 (0.699)	0.083
Encourage patient to believe in own ability by identifying his/her strength and progress in the rehabilitation	4.643 (0.497)	4.286 (0.611)	*0.025**[b]
Coach patient to relax e.g., by listening to music	3.167 (1.267)	3.500[a] (1.382)	0.305
Take time to talk with patient	4.143 (0.663)	4.429[b] (0.514)	*0.046*[b]
Take time to talk with family	4.071 (0.730)	4.357[b] (0.633)	*0.046*[b]
Patient teaching			
Give patient individualized teaching material upon admission	2.583 (1.240)	2.833[a] (1.193)	0.048
Secure patient teaching about stroke, its consequences and planned diagnostic tests and treatment	3.071 (1.269)	3.429[a] (1.089)	0.227
Secure family teaching about stroke, its consequences and planned diagnostic tests and treatment	3.077 (1.188)	3.615[a] (0.650)	0.052
Teach patient about the importance that the family participates with patient in rehabilitation	3.692 (1.437)	3.846[a] (1.068)	0.564
Teach family about the importance of their participation with patient in rehabilitation	3.667 (1.371)	3.917* (1.165)	0.257
Discharge planning			
Document discharge planning in patient electronic health records	2.833 (1.267)	3.917[b] (1.084)	*0.012*[b]
Assess patient's need for social support after discharge	4.214 (0.893)	4.143 (0.864)	0.739

Table 4 Difference in nurses' application of 30 quality indicators before and after implementation of the Stroke Nursing Guideline ($N = 14$) *(Continued)*

	Pre-test group M (SD)	Post-test group M (SD)	*p*-value
Assess mobility and self-care capabilities in discharge planning with			
a) FIM scale	1.727 (1.272)	2.000[a] (1.095)	0.317
b) scale in patient electronic health records	2.500 (1.650)	2.700[a] (1.494)	0.480
c) both FIM scale and scale in electronic patient health records	2.125 (1.356)	1.750 (1.165)	0.180
Conduct discharge planning interview, provide personalized information	3.000 (1.291)	2.923 (1.256)	0.739

[a]=differences, [b] = significant differences

care of hospitalized patients with stroke. Both the documentation and quality indicators showed that the nursing staff applied more mobility and ADL interventions, which included screening functional status and providing patients with exercise and training, and interventions focusing on education of patients and family all of which was supported by the qualitative findings. Also, satisfactory attention was paid to observing and assessing patients for the symptoms of depression which was also supported by the qualitative findings.

The feasibility and usefulness of the SNG, both the quantitative and qualitative findings showed that the nursing staff found the SNG useful. The findings of the focus group interviews also showed that the SNG recommendations were practical and easy to use and that it improved nursing care. The guideline layout was also illustrative and instructive for patients and family members.

Contrary to what was anticipated the facilitating factors on the BFAI instrument after implementation were lower for the subscales of "Innovation" and "Context" and no change was found for the "Professional" and "Patient" subscales. The qualitative findings, however, showed relatively positive experiences. The nursing staff judged the implementation to be successful, which was rated with the mean score of 7.5. They reported that they had taken an active part in the implementation. The implementation had brought a totally new view on mobilization in daily care and they found that consistent and coherent leadership had been provided during implementation. Through the SNG, essential components of rehabilitation had been defined and integrated into daily nursing care. Less visible aspects of nursing now received more attention and recognition. Explanation for this mismatch may be found in the questions of the BAFI which generally refer to the context and professional issues on the ward. At the time of the implementation of the guideline, severe organizational and budgetary restrictions were taking place.

The study showed improved documentation by the nursing staff after implementation of the SNG in 23 items focusing on screening and application of interventions. Significant improvements were found in three items focusing on *Mobility and ADL*. Likewise, parallel findings were found in that the nurses used the SNG more on the items *Mobility and ADL* indicators and with significant improvement in *Assisting and supervising patients with exercises according to physical therapists recommendations,* which was in line with the scores on the QIT. This was as well supported by the qualitative findings of the focus group interviews. The SNG provided consistency in care, particularly as the patients did exercises in the same way and there was more consistency in intensity and frequency of exercises. This indicates that the nursing staff generally paid more attention to mobility and ADL, conducting mobility assessments and actually mobilizing patients and providing them with exercises. This finding is in line with the findings of our earlier study investigating the feasibility of the CNRS-Guideline implemented in various stroke settings in the Netherlands [19]. It is however important to note that our study measured the documentation by the nursing staff and not the patient outcomes. However, various studies have shown that health care professionals pay limited attention to mobilizing patients with stroke. A recent intervention study comparing the amount of time spent in moderate-to high physical activity of stroke survivors on rehabilitation ward and acute stroke wards in Sweden showed that the amount of time spent in moderate-to high physical activity ranged between 24% on a rehabilitation ward and 23% on acute ward with no difference between the two groups. Compared to those in the acute setting, participants in the rehabilitation setting spent less time lying in bed, more time sitting supported out of bed, less time in their bedroom, and more time with a therapist (all adjusted $P < .001$) [56]. An observational behavioral mapping study, showed that stroke patients different medical wards were found inactive and alone for 19 to 15% of the time during the day and spent 46% of the time in therapeutic activities and 31% of the time in non-therapeutic activities. The family was present with patients 50% of the time during the day. The family presence with

Table 5 Nurses view of the usefulness of the Stroke Nursing Guideline and Implementation process (N=16)

Mean	Themes	Descriptions	Quotes
Usefulness of the Stroke Nursing Guideline			
Mean = 7.7 Range = 5.5–9.0	1. *Improved quality of care*	This theme described how the SNG generally improved nursing care generally.	"The SNG has improved the way we work, especially when assisting patients with moving and positioning". "The SNG has both improved the care, we think more about how we approach patients and how we help them with movement and ADL". "We do not only think about physical care but also psychological care, like depression". "We ask patients more about how they feel, – their psychological well being". "We make much more use of scales now". "We think more about the emotional par now and not only about the phhysical".
	2. *Content known to staff*	The content of the SNG was generally known to staff and already used to an extent in daily care.	"The SNG had not so much new things in it, but very good to have everything set up like this". "Some things were known to us already, but others are new, – like more emphasis on scales and of course depression".
	3. *Convenient and concise*	The SNG was convenient and teh text was concise, effortless to read, handy and practical, particularly for new staff and students.	"The recommendations are convenient and really very practical and fit very well with how we work on the wards". "The guideline is very easy to use. They (the recommendations) are not so extensive, they are short and easy to use". "The guideline is very easy to use". "We have had much new nursing staff and then it is very good to have the guideline".
	4. *More use of instruments*	Screening tools make staff focus more systematically on respective components e.g., depression, anxiety, risk of fall, and nutritional status, to be accurate in communicating about patients'symptoms, as well as to evaluate patients'progress.	"We use instruments more, especially the PHQ-9". "We are using the scales much more now with the guideline". "Now we use scales for most things like walking ability, falls, depression". "The scales are very easy and practical to use".
	5. More consistency	The SNG makes staff do things the same way, which is a quality issue, and with consistent intensity and frequency e.g., in doing physcial exercises with more rigorousness in the evenings and weekends.	"After following SNG and the training, we are all working in the same way, – there is much more consistency in how we move patients". "It is good that we are all working in the same way. For example when we are taking patients out of bed. Before the guideline we did this very differently".
	6. *Illustrative and instructive*	Concenring the layout of the SNG, the photos and diagrams are illustrative and instructive a) for staff who uses better ergonomics and b) for patients who are mobilized in a convenient and consistent way and c) for family members who can trust that patients receive the right care.	"We use the photos to show patients and family when patients go home for the weekend". "Good positions for in bed or when sitting, but also concerning the pain". "We can use the SNG much more with family".
Implementation process			
Mean = 7.5 Range 6.0–8.5	1. *Nursing rehabilitation defined and integrated*	Through the SNG, essential components of nursing rehabilitation have been defined and integrated into daily nursing care, e.g., going to the toilet is an opportunity to exercise stand up and sit down, rather than only being the fullfilment of a basic human need.	"The SNG is very compact. There is not so much new, – but it is much more clear now. Very clear guideline". "All these elements of nursing, like moving and ADL, screening for falls, mobility or depression, which were somehow hidden, are more clear now". "Integrating exercise into daily activities is so good for the patients". "We now say: Do you need to go to the toilet? Yes, great! That is exercise (laughs)". "We now do much more of general training, – activating patients".
	2. *Physical exercise Individualized*	Physcial exercise guidelines have made individualized instructions from physical therapists less needed.	"The mobililty ADL part of the guideline is very good, gives good instruction on how to mobilize patients. Also positioning, – especially the arm". "Very good to have the photo's on mobility and positioning, – we are becoming much better in helping and instructing on how to move and do excercies".
	3. *Enhanced patient and family teaching*	Enhanced patient and family teaching, with particularly good teaching material	"It is much better to teach patients and family about mobility and integrating exercises into daily activities when having this written down and digital".

Table 5 Nurses view of the usefulness of the Stroke Nursing Guideline and Implementation process (N=16) *(Continued)*

Mean	Themes	Descriptions	Quotes
		(booklet), bringing forth a request for structured family interviews.	"I like to have this in a printed map, which you can take with you and show to patients and family".
	4. *Coherent and consistent leadership*	Leadership of the charing group during implementation of the SNG was coherent and consistent.	"The implementation went very well". "The implementation was well led by the chairing group, – they did a very good follow up on things". "They (the charing group) really were in charge of things".
	5. *Improved staff education*	The SNG resulted in good/improved staff education, which needs to be repeated consistently throughout the care continuoum.	"The educational and training sessions for staff were very good, – but it needs to be repeated regulary". "It is much better to have an active training like this, – you need to do the things and not only read about them". "We need to have the training sessions repeated regularly to refresh things, – you tend to forget".
	6. *Less visible nursing care received attention*	Through the SNG, previous less visible aspects of nursing care have received attention and recognition among all staff, particularly its contribution to the success of patient rehabilitation.	"Posters with photo's on positioning and mobilizing of patients have been put on the walls for patients and famly as well for staff. Nursing and what we do in rehabilitation is now more visible for all staff". "The guideline has made elements of nursing care much more visible to other staff as wel". "What we nurses are doing in rehabilitation, like mobilizing and stimulating patients to exercise is now much more visible to the other staff".

the patient and the patient's moderate dependence in daily activities were positively associated with their activity levels. The authors concluded that the presence of family members with the patients during hospital stay may be a significant resource for encouraging patients to be more active [57]. Two smaller studies showed that patients in Dutch nursing homes were inactive and alone for up to 49% and 60% of the day [58, 59]. Therapeutic time use was significantly related to improved functional status; patients with higher functional status spent more time on therapeutic activities [58]. It is highly important that nursing staff activate patients and provide them with opportunities to do exercises in between physical therapy and occupational therapy training sessions and the findings of this study suggest that the SNG is exactly facilitative of that.

Depressive symptoms were only measured post-intervention as the nurses did not conduct screening of depression prior to the implementation of the SNG. After implementation of the SNG, the application of the SNG recommendations was quite satisfactory as three out of four items on the QIT were used. This was supported by the qualitative findings of the focus group interviews which showed that the nurses paid more attention to depression and they used the PHQ-9 for screening. In our earlier study, investigating the feasibility of the CNRS-Guideline implemented in various Dutch stroke settings, we found that the nurses acknowledge the importance of assessing and acknowledging the symptoms of depression, but they rarely used recommended instruments for screening depression or evidence based interventions [19]. Depression after stroke is frequent and strongly impacts patients' recovery as patients have worse functional outcome, lower quality of life and are at more risk of dying [27, 28, 60, 61]. There is however growing evidence for the beneficial effects of physical activity [62], self-efficacy [18, 63] and social support [64] all of which can be used by nurses in the daily care of patients with stroke.

This study shows that after the implementation of the SNG the nurses reported enhanced patient and family teaching and that they provided good teaching material that focused on patients and family. This extends

Table 6 Difference on the Barriers and Facilitators Assessment Instrument before and after. implementing the Stroke Nursing Guideline ($N = 20$)

	Item	Pre-test group	Post-test group	*p*-value
	($N = 27$)	M (SD)	M (SD)	
Innovation	6	4.017 (0.492)	3.755 (0.509)	*0.019* [a]
Professional	10	3.874 (0.445)	3.821 (0.675)	0.074
Patient	6	3.392 (0.630)	3.415 (0.563)	0.055
Context	5	2.632 (0.547)	2.474 (0.542)	*0.001*[a]

[a]A *p*-value cursive indicates significant difference between groups

previous research which has pointed to the importance of patient and family education albeit with a lack thereof [40]. A meta-analysis including 21 trials (2289 patients and 1290 caregivers) and assessing the effectiveness of education provided to patients with stroke and their caregivers, provided evidence that education improves patient and caregiver knowledge of stroke, aspects of patient satisfaction, and reduces patient depression scores. The authors recommend that, although the best way to provide education is still unclear, there is some evidence that strategies that actively involve patients and caregivers in education and includes planned follow-up for clarification and reinforcement have a greater effect on patient mood [65].

Although the study showed improved documentation and use of the SNG on items focusing on mobility and activities of daily living, depressive symptoms, patient teaching and discharge planning, the results of the study show that the implementation and use of the SNG still can be improved on items focusing on pain or falls. The question remains as to why the other elements of the SNG were not as well applied. The nursing staff generally judged the guideline to be practical and easy to use. Earlier studies, however, have reported similar results. Metzelthin and colleagues [66] investigated the implementation of a nurse-led interdisciplinary primary care approach using a process evaluation and concluded that some parts of the program were insufficiently executed [66]. Similar findings were reported in a mixed method study investigating care delivery of a nurse-led intervention, where some time-consuming interventions were less often applied than other interventions [67]. A feasibility study of a fall-prevention program, where interventions that required more knowledge, communication and extra activities were implemented the least. The absence of materials and knowledge about falls prevention were important determinants of the non-implementation of certain interventions [68]. However, given the complexity of guidelines like the SNG, implementation is challenging and needs continuous education of nursing staff and other professionals. It is highly important to continuously monitor and evaluate the implementation and use of the SNG and to verify the extent to which the SNG recommendations are delivered as intended. Further research is warranted into the development and testing as well as implementation and translation of complex interventions like the SNG into the daily care of patients with stroke.

Strengths and limitations

To appreciate the findings of this study, some limitations need to be considered. The fact that the study took place on only two wards within the same hospital and the fact that the sample of nurses participating was a small convenience sample, which was due to intense workload of nurses, unprecedented staffing shortages, including organizational changes occurring at the same time, and is in line with earlier studies [19, 69, 70]. Therefore, caution is indicated in generalizing the results of this study to other nurses in different organizational settings. However, the demographic data from both nurses and patients participating in our study do reflect the Icelandic population. Although we conducted thorough translation procedure of the instruments used no psychometric testing was conducted. The researchers participated in the development of the guideline and the implementation process, which could have limited objectivity. However, because of the quality assurances taken, the quality of the data can be ensured. The implementation strategies used was based on the literature, with active and multifaceted aspects, which benefited the study [44, 45]. The mixed method design provided rich data. The findings of the qualitative part were illustrative of the findings of the quantitative findings of the study to which they provided more depth.

Some may, however, consider the design of the study to be limited by the fact that we measured difference in the nurses documentation of SNG key interventions before and after implementation and not difference in patient outcomes. It is important to note that this study was not an outcome study, but a feasibility study investigating the usability of the SNG and documentation of interventions is an important parameter in measuring usability. Further, robust outcome studies are warranted to investigate the effects of the SNG on various patient outcomes including larger samples with a longer follow-up period.

Conclusions

The findings of this study indicate that implementation of the SNG improved patient care as illustrated in the patient electronic documentation system, nurses answers on the Quality Indicators Tool and focus group interview with nursing staff. Most improvements were found on assessing mobility and ADL and patients were activated more and they as well participated more in exercise and training. The nursing staff gave more education to patients and families and they paid more attention to the symptoms of depression and screened patients for depression. Using the SNG, the essential components of rehabilitation were defined and integrated into daily nursing care. The nursing staff found the SNG feasible and that it was practical and easy to use and it improved nursing care. The guideline layout was illustrative and instructive for patients and family members. The nursing staff judged the implementation of the SNG to be successful and they generally took an active part in the implementation. The SNG needs to be further developed and robust research needs to be conducted to investigate

the effects of the SNG on the outcomes of patients with stroke in various settings where patients with stroke reside. Thereby we may be able to improve the clinical outcomes of patients with stroke.

Shared decision-making in stroke: an evolving approach to improved patient care

ABSTRACT

Shared decision-making (SDM) occurs when patients, families and clinicians consider patients' values and preferences alongside the best medical evidence and partner to make the best decision for a given patient in a specific scenario. SDM is increasingly promoted within Western contexts and is also being explored outside such settings, including in China. SDM and tools to promote SDM can improve patients' knowledge/understanding, participation in the decision-making process, satisfaction and trust in the healthcare team. SDM has also proposed long-term benefits to patients, clinicians, organisations and healthcare systems. To successfully perform SDM, clinicians must know their patients' values and goals and the evidence underlying different diagnostic and treatment options. This is relevant for decisions throughout stroke care, from thrombolysis to goals of care, diagnostic assessments, rehabilitation strategies, and secondary stroke prevention. Various physician, patient, family, cultural and system barriers to SDM exist. Strategies to overcome these barriers and facilitate SDM include clinician motivation, patient participation, adequate time and tools to support the process, such as decision aids. Although research about SDM in stroke care is lacking, decision aids are available for select decisions, such as anticoagulation for stroke prevention in atrial fibrillation. Future research is needed regarding both cultural aspects of successful SDM and application of SDM to stroke-specific contexts.

Shared decision-making (SDM) is an increasingly referenced and lauded approach to medical decision-making in Western countries, and its use is also spreading to other contexts including China[1] and Malaysia.[2] SDM is a partnership between patients (and families, where appropriate) and clinicians that considers patients' values and preferences alongside medical evidence to make the best decisions for a given patient in a specific scenario.

In Western countries, arguments for SDM often focus on principles of autonomy and self-determination, particularly in the setting of clinical uncertainty. For many decisions, there is not a 'right' answer; SDM enables patients and families to choose the best option for them based on individual values, goals and considerations such as mechanism of administration, cost and side effect profile.

Arguments supporting the use of SDM go beyond these principles, however. Research suggests that SDM results in improved knowledge/understanding, satisfaction and trust,[3] which are hoped to also lead to better health outcomes. Decision aids (DAs)—tools that guide patients, families and clinicians through the SDM process—increase knowledge, lower patients' decisional conflict, reduce patient passivity in decision-making and the number of patients unable to decide, and result in more decisions for less-aggressive care.[4] Research to date has focused more on these short-term outcomes of SDM rather than its long-term impact on health outcomes.[3 5 6] A conceptual model of SDM, however, suggests that SDM can result in short-term, mid-term and long-range benefits for patients, clinicians/other healthcare professionals, organisations and healthcare systems, including improved decision-making, satisfaction, patient experiences, trust, health outcomes, cost-effectiveness and resource utilisation, along with decreases in litigation and professional burnout.[6]

APPROACHES TO SDM

SDM likely best occurs in the setting where a physician and a patient have an established relationship such that the physician knows the patient's values and goals, informing how options are described and weighed during SDM.[7] Even in the acute setting, such as the emergency department or during hospitalisation, understanding a patient's background (eg, employment) and values prior to formal decision-making can provide important context for decisions.

There are multiple models for SDM with different numbers of outlined steps.[8–10] When a clinical decision is needed, SDM starts by engaging patients and key supports in the process (table 1). This step requires the clinician to understand who the patient desires to

Table 1	Steps to shared decision-making
Step 1	Engage patients (and other decision makers, if appropriate) in the decision-making process
Step 2	Describe the decision and the options available, including each option's potential benefits and risks, how the options are different and what is unknown about the options (the uncertainty)
Step 3	Further assess the patient's values and goals, specifically as they relate to the available options
Step 4	Make the decision together

participate in decision-making, such as a family member. In situations where a patient is incapacitated and unable to participate, SDM occurs with the surrogate decision maker. Even if a patient ultimately desires to defer the decision to a physician or family member, it is important to actively engage him/her in the SDM process.

Once patients and families are engaged, the second step (table 1) is specifically describing the decision and outlining the different options. In describing the different options, clinicians should use the available medical evidence to inform patients about the potential benefits and risks. It is also important to highlight when there is something unknown about the options (uncertainty) and to describe how the options are distinct. Differences between options include potential benefits and harms and considerations such as cost and invasiveness. This discussion should be individualised—for example, the balance of benefits and harms of clopidogrel for secondary stroke prevention will be different between a person with a prior history of bleeding gastric ulcers and a person with no such medical history.

Once the evidence is presented, the intersection between the options and the patient's values and goals is explored (step 3, table 1). If a patient's circumstances, values and goals were known prior to the initiation of SDM, the presentation of the options in step 2 should occur in that context. For example, if a patient lives alone and prioritises continued independence, the potential benefits and risks of each intervention are specifically presented with a reference to the likelihood of maintaining independence (eg, from successful treatment) or putting it at risk (eg, due to side effects). Regardless of prior knowledge of patient values, in step 3 a patient's values as they specifically relate to the decision are explored. What is most important to the patient in this situation—expected functional recovery? Amount of risk? Cost?

Finally, a decision is made. Ideally, the patient makes the decision with the help of those friends or family members whom he or she has chosen for involvement. Sometimes patients prefer clinicians to make final decisions. In these circumstances, patients often still express a desire for participating in SDM,[11] but request that the clinician select the best strategy after discussion. When the patient defers to clinicians, the burden is on the physician to target the decision to the patient's stated values and goals, thus still using SDM to make the best individualised decision for that patient in that circumstance.

In many circumstances, particularly those encountered in the outpatient setting, re-evaluation is an important component of SDM. Anticipated ongoing benefits and risks may change based on the development of comorbidities; patients' values and priorities may change based on their experiences with a medication or shifting life circumstances. In the outpatient clinic, for example, decisions regarding anticoagulation for secondary stroke prevention in the setting of atrial fibrillation should be reassessed over time. This is in contrast to certain acute stroke decisions, such as those regarding tissue plasminogen activator (t-PA), where the window for SDM is small, with little opportunity for re-evaluation.

Values and goals

Within SDM, values tied clearly to diagnostic or therapeutic options such as efficacy, toxicity, quality of life, convenience and cost are often emphasised.[12] Other values and goals may also inform patient decisions, however, and these can be critical to SDM.[13] Global values reflect life priorities or beliefs, which may be religious or cultural in origin; these values impact all decisions. Global values can also represent value traits, such as risk aversion or a desire to try the 'new' thing, which also influences approaches to decision-making.[13] External values reflect a patient's choice to consider others' values and preferences when making a decision.[13] This occurs in Western cultures but may be more important in other cultures, such as in mainland China where family involvement in decision-making can reflect mutual benevolence and the Confucian ideal of family harmony,[14] or places like Pakistan where the norm is family–doctor–patient triadic decision-making.[15] Finally, situational values reflect context-specific factors that influence a decision differently now than in the past or future, such as an upcoming event (eg, a wedding) that may impact how long a patient is willing to remain in the hospital or rehabilitation.[13]

The role of evidence-based medicine

Although SDM is often emphasised in discussions of personalised and patient-centred care, it is critical to note that this process relies on evidence-based medicine. Evidence-based medicine is foundational to step 2 of SDM (table 1), where patients, families and clinicians discuss the evidence (or uncertainty/lack of evidence) of benefits and harms for each potential option. It is only by knowing the available evidence that patients and families can make informed decisions. To present this evidence, clinicians can reference original research or use tools such as DAs, systematic reviews or evidence-based guidelines, each of which summarises known evidence in response to a specific question or choice.

SDM AND STROKE

Most recent publications on SDM in stroke care focus on oral anticoagulation for stroke prevention in atrial fibrillation.[16–20] This is a decision where SDM clearly plays an important role given differences in individual risks based on comorbidities, multiple options with different potential benefits, risks, costs and time requirements (eg, for international normalized ratio [INR] monitoring), and obvious value assessments relating to potential outcomes such as stroke and bleeding.

Less research exists for other decisions relating to stroke, and currently available DAs may not meet decision aid standards.[21] A 2013 review of patient tools designed for decision-making regarding thrombolytic treatment identified that available tools lacked key development stages, presented outcome probabilities poorly and failed to completely describe potential benefits and risks.[22] Subsequently, the COMPuterized decsion Aid for Stroke thrombolysiS (COMPASS) tool, a computerised DA for thrombolysis in acute stroke, was developed with clinicians, patients, families and modelling techniques. Using the tool took a median time of only 2.8 min in early pilot testing, but additional study is required.[23 24] DAs have particular potential for improving care in this emergent setting, where SDM is challenged by the time limitations for effective thrombolysis, the need to engage patients and families and convey knowledge in the context of the shock and effects of an acute stroke, and the need to incorporate personal values into a decision that relies heavily on physician expertise.[25]

Barriers to SDM

Research on barriers to SDM is largely conducted in Western contexts. Identified barriers to SDM include physician and patient attitudes towards SDM,[26 27] lack of familiarity and experience with SDM,[26] lack of continuity of care,[27] physician knowledge regarding evidence,[26 27] the physician–patient relationship,[27] insufficient explanations,[27] use of medical terminology,[27] the ability of patients and families to understand and use health-related information (health literacy),[27 28] lack of resources[26 27] and time.[10 26 27]

Research regarding SDM in China is extremely limited, but identified barriers overlap with those described elsewhere and include lack of resources, time, physician communication skills, patient–physician relationships, the health literacy of patients and families, and unrealistic patient and family expectations.[1] Despite these barriers, a recent study found it feasible to implement the use of a statin DA for cardiovascular risk reduction in two teaching hospitals in Northern China.[29] Additional barriers identified in this study included lack of privacy for uninterrupted discussions, family dominance within some encounters, lack of applicability of data within Western DAs to Chinese contexts, and low health literacy requiring additional cardiovascular education in order for patients to effectively use the tool.[29]

Facilitators of SDM

The most commonly described facilitators of SDM are clinician-related: clinician motivation and the perception that SDM improves the clinical process and patient outcomes.[26] Patient-identified facilitators include continuity of care, good relationships between patients and clinicians, trust, adequate time, engagement of various members of the healthcare team (eg, nurses, in addition to doctors), a sense of partnership, encouragement of patients to participate and ask questions, the provision of sufficient information, use of plain language, and patient engagement and ownership in the process.[27]

DAs are practical facilitators of SDM, although they are insufficient on their own and have some limitations.[27] DAs are useful for addressing barriers to SDM, such as lack of familiarity with SDM, physician knowledge regarding evidence, and provision of sufficient and understandable information, as DAs walk clinicians, patients and families through the SDM process and describe the medical evidence in plain language, often using visual aids.

Although there are few published stroke-related DAs, approaches exist for helping clinicians develop tools for commonly encountered decisions, such as Option Grids.[30] In the absence of formal tools, other patient education materials can be helpful in promoting step 2 of SDM, such as those available through neurology and stroke organisations. Ideal tools will be culturally and context-sensitive, something of particular importance as SDM spreads to non-Western contexts.[1 29]

CONCLUSIONS

SDM is an increasingly promoted approach for patients, families and clinicians to partner to make the best medical decisions for each individual in a particular moment by using the best medical evidence. Although long-term benefits for patients, families, clinicians, hospitals and health systems have yet to be explored, SDM has known benefits on decision-making and satisfaction and has the potential for improving other outcomes as well. Every decision within stroke care has potential for improvement with SDM, whether relating to thrombolysis, goals of care, diagnostic assessments, rehabilitation strategies or secondary stroke prevention. Although SDM is necessarily context-specific, development of DAs for commonly faced decisions within vascular neurology may improve stroke care. Future research is needed regarding the cultural elements of SDM in general and also within the field of stroke.

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