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Review Article

Infection as a Key Determinant of Readmission in Stroke Patients: A Systematic Review and Meta-Analysis

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Abstract

Background: Accurately identifying the relationship between infection and the readmission of stroke patients leads to emphasis more the corresponding strategies. We aimed to determine the relationship between infection and readmission in stroke patients.

Methods: This systematic review and meta-analysis was based on PRISMA 2020 guidelines. A comprehensive search was performed across multiple databases, including PubMed, Web of Science, CINAHL, Scopus, and Google Scholar, using keywords such as "stroke," "readmission," "recurrence," "re-hospitalization," and "infection" up to 2024. The rate of readmissions due to infection, along with the Odds Ratio (OR) for infection, was calculated using a random effects model via Comprehensive Meta-Analysis V.2 software.

Results: Based on the reviewed studies, the 30-day readmission rate of stroke patients due to infection ranged from 6.5% to 30.0% and the one-year readmission rate ranged from 5.1% to 24.5%. Also, infection is an important risk factor in the readmission of stroke patients based on cohort studies (RR 1.38, 95% CI: 1.16-1.65, $P<0.001$), case-control (OR 1.68, 95% CI: 1.16-2.42, $P= 0.006$) and descriptive-analytical (OR 1.31, 95% CI: 1.07-1.59, $P= 0.008$).

Conclusion: The readmission rate of stroke due to infection is high and tackling infection-related readmissions in stroke patients necessitates a holistic strategy that combines clinical care, technological advancements, and education. More studies are needed in this field.

Keywords: Risk factors; Readmission; Stroke; Cerebrovascular accident; Infection

Introduction

Readmission is a significant adverse outcome in patients with chronic conditions, particularly among those who have experienced a stroke. This concern is compounded by the associated increases in morbidity and mortality rates (1). Readmission rates among stroke patients can be alarmingly high, with estimates ranging from 31% to 56.1% within the first year following discharge (2). Notably, 17.4% of these readmissions occur within the first month (3), and approximately half

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take place within the first three months post-discharge (4). While the high rate of readmission poses a serious challenge in managing stroke patients, understanding the underlying causes is equally critical (2, 5).

One prominent non-vascular risk factor contributing to the frequent readmission of stroke patients is infection (2, 6). Infections can arise during hospitalization or after discharge, posing a continuous threat to patient recovery (7-9). Stroke patients exhibit unique vulnerabilities that differentiate them from other hospitalized populations. Factors such as dysphagia, impaired gag and cough reflexes, aspiration risk, dehydration, immobility, and respiratory muscle weakness significantly heighten their susceptibility to respiratory infections (10). Additionally, urinary tract infections (UTIs) are prevalent due to factors such as catheter use, incontinence, and urinary retention (10). Unlike other patient populations, stroke survivors may have prolonged hospital stays due to complications like aspiration pneumonia, urinary tract infections, and pressure ulcers, which are exacerbated by their neurological deficits (2). The unique clinical profile of stroke patients, characterized by neurological deficits and complications, sets them apart from other long-term hospitalized patients. Furthermore, the acute nature of stroke can lead to rapid deterioration in health status, making them more susceptible to nosocomial infections (7, 11).

Despite the clear association between infections and readmission rates, the depth of discussion regarding their significance and prevention remains insufficient (6, 10, 12). In addition, many studies focus on short-term readmission rates, particularly within the first month post-discharge. However, this study will take a longitudinal approach by entering the observational studies, examining readmission rates over a more extended period (up to one year). This perspective will allow for a comprehensive evaluation of how infections affects long-term recovery and readmission in stroke patients. Furthermore, there is limited information available on the extent to which infections contribute to readmissions specifically in stroke patients compared to other patient populations (7, 13, 14). Moreover, despite recognizing the relationship between infections and readmissions, few studies have proposed actionable prevention strategies tailored specifically for stroke patients. This study aims to not only identify the problem but also recommend evidence-based interventions that healthcare providers can implement to reduce infection rates and subsequent readmissions (7, 11). By addressing these gaps, this study will contribute novel insights into the interplay between infections and readmission in stroke patients, ultimately aiming to improve patient outcomes and inform clinical practices.

Consequently, this study aimed to evaluate the relationship between infection and readmission in stroke patients, thereby highlighting the need for focused interventions in this vulnerable population.

Materials and Methods

This study was designed and conducted to determine the relationship between infection and readmission of stroke patients as a meta-analysis from August 2022 to November 2023. The structure of the study was designed based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

Data Collection

For this purpose, studies published in reliable databases PubMed, Web of Science, Scopus, Cochrane Library CINAHL, and Google Scholar search engine were done until November 2023 using search strategy:

((((Stroke) OR (Cerebrovascular Disease)) OR (Cerebrovascular Accident)) AND (((Infection) OR (Urinary Tract Infection)) OR (Pneumonia))) AND (((Readmission) OR (Recurrence)) OR (Re-hospitalization)). The sources of the articles were also searched.

Inclusion and exclusion criteria and Quality Assessment

The study inclusion criteria include readmission of stroke patients, studies focused on readmis-

sion of stroke patients due to any type of infection, cohort study design, case-control, and descriptive-analytical, full-text articles and the language was English. If a study does not have full text, the responsible author of the article was requested via email, if he did not respond to the email for more than 2 weeks, he was excluded from the study (n=1). To ensure the coherence of the findings, the electronic search was conducted by the second researcher separately. Duplicates were removed. Any disagreement between the researchers was investigated and resolved through discussion until the desired satisfaction was reached. The final included studies were subjected to quality assessment. Descriptive-analytical studies are evaluated using the JBI (Joanna Briggs Institute) tool, and observational studies (case- control and cohorts) are evaluated using the Newcastle-Ottawa scale (NOS) (15). The JBI tool consists of 8 questions to determine the possibility of bias in the methodology of descriptive-analytical studies. Each question was given a score of 0 (no or unclear) or 1 (yes). In the total of questions, a score of 6 and above indicates high quality, 4 to 6 indicates moderate quality, and less than 4 indicates low quality (16). The Newcastle-Ottawa scale (NOS) tool also includes 8 questions for case-control studies and 8 questions for cohort studies. Both types of NOS tools have three domains: selection (4 questions), comparability (1 question) and Outcome (3 questions). Questions 1 and 3 are assigned the categories of selection and outcome, and the only question in the area of comparability is assigned 2 stars, and one star is assigned to the rest of the questions. If the study gets 3 or 4 stars in the category of selection, 1 or 2 stars in the field of comparability, and 2 or 3 stars in the category of outcome, it is considered high quality. If the study gets 2 stars in the selection category, 1 or 2 stars in the comparability category, and 2 or 3 stars in the outcome area, it is considered of moderate quality. If the study gets zero or one star in the category of selection and zero star in the category of comparability and zero or one star in the category of outcome, it is considered to be of low quality (15, 17). From these studies, high and moderate quality were selected.

Data extraction

Data extraction included authors, year of publication, design and purpose, sample size, follow-up and readmission rate for infection, main results. The study selection, data extraction, and reporting of results were all based on the preferred reporting items for systematic reviews and meta-analyses (PRISMA) checklist (18).

Data Synthesis

Studies were synthesized descriptive and 30-day and one-year readmission rates of stroke patients due to infection were reported. These findings were presented in a table based on the authors' names, year, type of study, sample size, readmission rate due to infection and main results.

Statistical Analysis

As the included articles in the final analysis were prospective (cohort) and retrospective (case- control) observational and descriptive- analytic studies, the pooled effect size was estimated using risk ratio (RR) for cohort studies and odds ratio (OR) for case-control studies, and the 95% confidence interval (CI) was also calculated. In addition, it is reported separate infection-caused readmission rate for 30-day and 1-year. It has implemented a random effect model, which allows ORs to be included in the corresponding input. Random-effect models are more appropriate than fixed-effect models when the number of studies included in the meta-analysis is low (< 10) (19).
It performed an initial analysis of all available data to arrive at a single pooled estimate. Comprehensive Meta-Analysis V.2 software has been used to calculate the summary estimate and plot of effects (20). The Q statistic, Tau^2 and I^2 value was used to assess heterogeneity. I^2 values of 25% are considered as low-heterogeneity, 50% as moderate-heterogeneity, and 75% as high-heterogeneity (19). A P value of <0.05 was considered statistically significant.

Results

From the 2533 titles of determined articles, after screening and removing duplicates, 14 articles were included in the study for final analysis. Of these, 8 were cohort, 3 were case-control, and 3 were descriptive-analytic (Fig. 1).

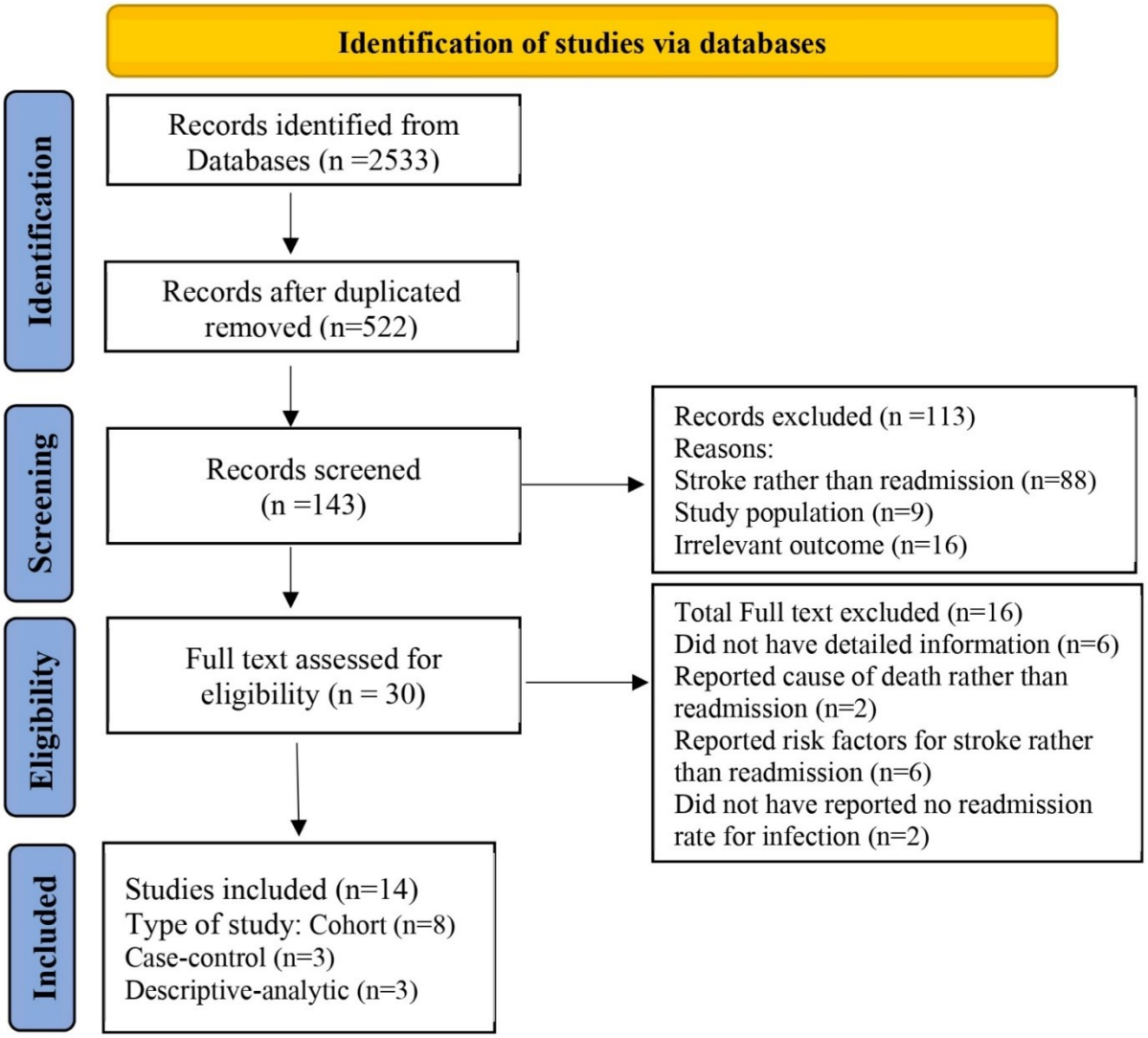

Fig. 1: PRISMA flow diagram of the search process

Results of literature search and statistical analysis:

Based on reviewed studies, the 30-day readmission rate of stroke patients due to infection ranged from 6.5% to 30.0% (21, 22) and one-year readmission from 5.1% to 24.5% was reported (4, 7) (Table 1).

Table 1: Summary of included studies

No.	Authors (year of publication)	Country	Study design	Purpose	Sample Size	Follow-up	Readmission rate (%) for Infection	Main results
1	Kilkenny et al (2013) (21)	Australia	Descriptive-Analytic	To describe the factors associated with 28-day readmission after hospitalization for stroke	3328	28-day	6.5	The majority reasons for readmissions are stroke or cardiovascular disease and infections.
2	Lee et al (2013) (23)	Taiwan	Cohort	To characterize disease burden by evaluating readmissions, mortality, and medical cost during the first year after acute stroke under the National Health Insurance (NHI) program	2128	1-year	7.3	Readmissions were mainly because of acute recurrent stroke or the late effects of previous stroke, respiratory disease/infections, heart/circulatory disease, and diseases of the digestive system.
3	Strowd et al (2015) (24)	US	Case-control	To identify those factors identified at discharge that are most strongly associated with 30-day readmission in patients with ischemic and hemorrhagic stroke	165	30-day	21.5	Significantly higher rates of pneumonia ($P = .029$), acute renal failure ($P = .02$), and urinary tract infection (UTI; $P = .017$) were present in cases during incident readmission.
4	Bjerkreim et al (2015) (4)	Norway	Cohort	Assessing frequencies, causes, and factors associated with early and late unplanned readmissions within 1 year after discharge from ischemic stroke hospitalization	1175	1-year	24.5	Infections (pneumonia and UTIs) were the most common cause of readmission.
5	Lord et al (2016) (14)	US	Cohort	To assess the hypothesis that infections are associated with a majority of 30-day readmissions to acute care hospitals after ICH	3550	30-day	22	Of all readmissions, 22% was related to infection.
6	Rohweder (2017) (9)	Norway	Cohort	to examine the hospital readmissions in a 10 year follow-up of stroke complications and to focus on their frequency, their causes and their timing	243	10-year	17.3	17.3% of readmissions were caused by infection.
7	Nouh et al (2017) (22)	US	Case–control	To evaluate etiologies and predictors of 30-day readmissions and determine the associated mortality risk	1544	30-day	30.0	The most common etiologies for readmission were infection (30%), recurrent stroke and TIA (20%), and cardiac complications (14%).
8	Boehme et al (2018) (11)	US	Descriptive-Analytic	To identify common infections occurring during the stroke stay are associated with 30-day readmission	319317	30-day	12.1	Patients with infection during their stroke admission had a 21% higher odds of being readmitted

Table 1: Continued …

								than patients without any type of infection (adjusted OR 1.21, 95%CI 1.16–1.26). The association between infection and readmission was similar with an increased odds of readmission (adjusted OR 1.23, 95%CI 1.18–1.29).
9	Miller et al (2019) (7)	US	Cohort	To assess the association of infections diagnosed during delivery hospitalizations with risk of readmission for postpartum stroke of any type	17215614	1-year	5.1	Women with infections had higher risk of readmission for postpartum IS (aRR, 1.75; 95% CI, 1.37–2.22).
10	Bjerkreim et al (2019) (25)	Norway	Cohort	To study the five-year incidence and risk of all-cause readmission, cause-specific readmission and mortality after IS or TIA by stroke subtype	1453	5-year	14.6	The five-year incidence of all-cause readmission was 72.6% with infections, cardiac disease, stroke-related events and fractures as the most frequent causes.
11	Xu et al (2020) (10)	China	Cohort	To investigate the association of infection with short- and long-term risk of recurrent stroke in patients with ischemic stroke.	789596	1-year	10.4	Patients with infection had a higher risk of stroke recurrence during hospitalization compared with patients without infection (10.4% versus 5.2%; adjusted odds ratio, 1.70 [95% CI, 1.65–1.75]; *P*<0.0001).
12	Qiu et al (2021) (8)	China	Case–control	To investigate predictors and causes of 30-day readmission after AIS	504	30-day	28.8	The most common causes for 30-day readmission were infection (28.8%) and recurrent stroke and TIA (22.8%).
13	Ang et al (2021) (26)	US	Descriptive-Analytic	To assess the risk of 28-day readmissions among stroke patients in Malaysia	23507	28-day	20.7	The leading causes for readmissions were recurrent stroke, pneumonia and sepsis.
14	Zhou et al (2023) (27)	US	Cohort	To examine readmissions rates, diagnoses at readmission, and risk factors associated with readmission following acute ischemic stroke (AIS) in a large United States (US) administrative Database	273811	1-year	19.9	The most common causes of readmissions were stroke, followed by sepsis and acute renal failure.

Also, based on meta-analysis, infection as an important risk factor in readmission of stroke patients based on cohort studies (RR 1.38, 95% CI: 1.16-1.65, *P*<0.001) (Fig. 2), case-control (OR 1.68) , 95% CI: 1.16-2.42, P= 0.006) (Fig. 3) and descriptive-analytical (OR 1.31, 95% CI: 1.07-1.59, *P*= 0.008) (Fig. 4) were identified.

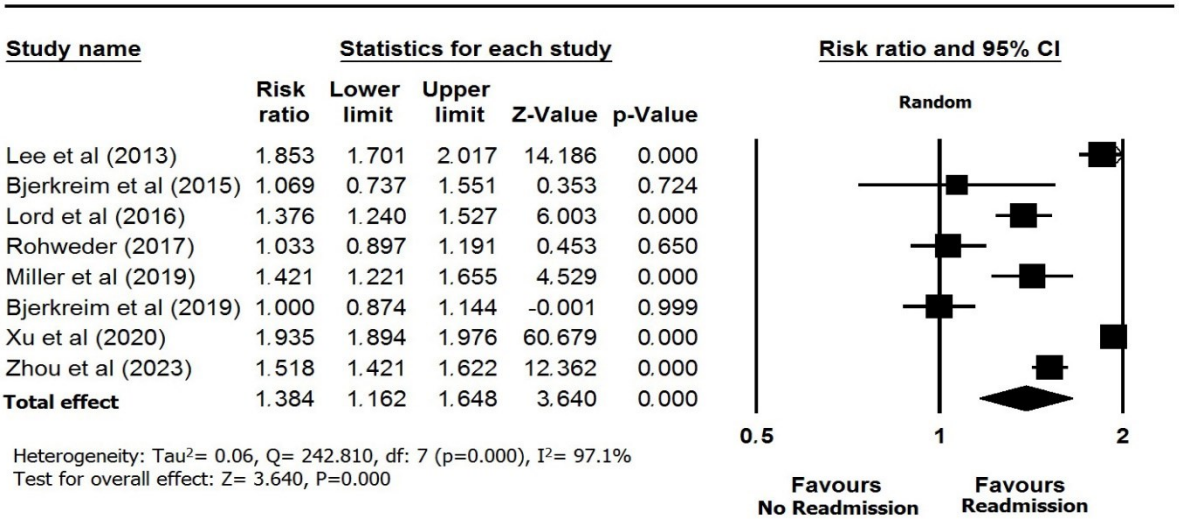

Fig. 2: Influence of infection on readmission in stroke patients based on cohort studies

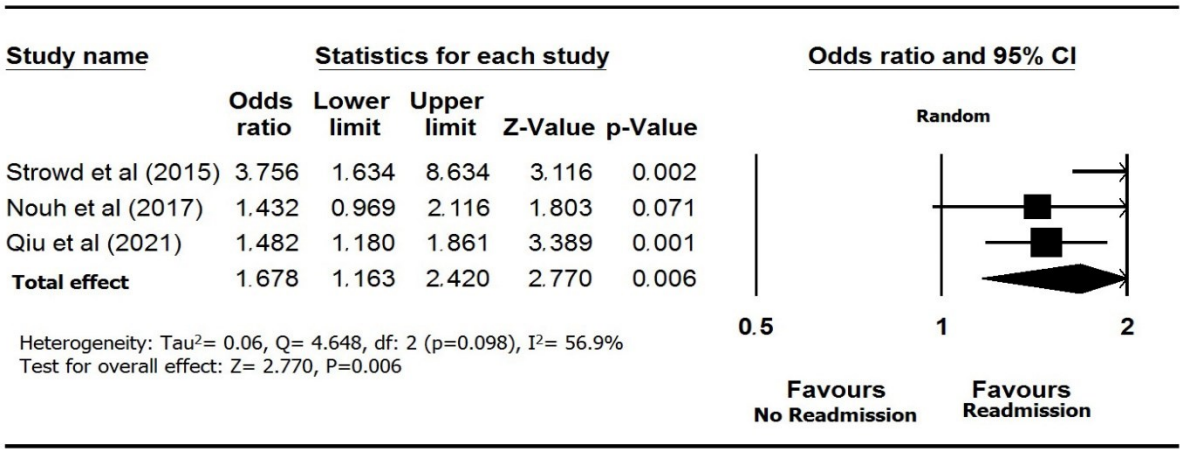

Fig. 3: Influence of infection on readmission in stroke patients based on case-control studies

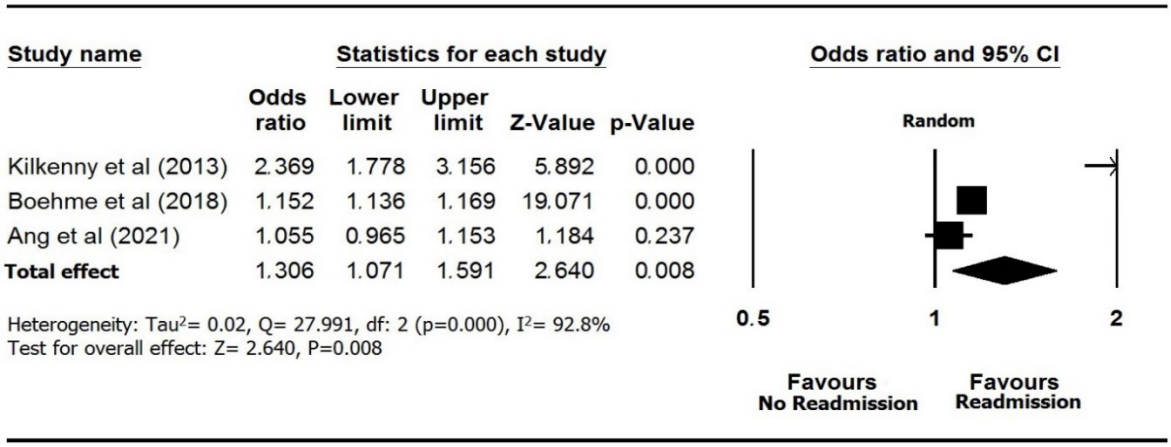

Fig. 4: Influence of infection on readmission in stroke patients based on descriptive-analytical studies

Quality assessment

The included articles were of moderate quality (n=10) or high quality (n=4) (Appendices).

Publication bias

For publication bias study in a meta-analysis by funnel plot test, there should be at least 10 articles, fewer studies might not give sufficient power to the test and may not detect real asymmetry (28). Thus, we did not report publication bias in this study.

Discussion

According to our research, this is the first meta-analysis to determine the relation of infections for 30-day and 1-year readmission in patients with stroke. Although several studies have investigated the infections for readmission in stroke patients (8-10, 12, 21-23). However, despite the significant importance of this factor, so far no meta-analysis study has been published in this field. In recent years, the relationship between infection and stroke readmission has garnered significant attention within the medical community. The findings of our systematic review and meta-analysis underscore the critical interplay between these two health challenges, highlighting that infections, particularly pneumonia and urinary tract infections, are prevalent among stroke patients and are associated with increased rates of readmission (29). This phenomenon not only complicates patient recovery but also imposes a substantial burden on healthcare systems.

To address the challenge of infection-related readmissions in stroke patients, it is essential to implement strong, integrated strategies that encompass prevention, early detection, and management of infections. One promising approach involves enhancing the multidisciplinary care model. By fostering collaboration among neurologists, infectious disease specialists, rehabilitation teams, and nursing staff, healthcare providers can create a more comprehensive care plan that prioritizes infection prevention from the outset (30). For instance, a study (31) demonstrated that implementing standardized protocols (such as the use of bundle care strategies, which include measures: early mobilization, proper catheter management, and oral hygiene (32)) for early mobilization and respiratory care significantly reduced the incidence of pneumonia in stroke patients.

Moreover, leveraging technology to monitor and manage infection risk can be transformative. The integration of electronic health records (EHR) with predictive analytics can help identify high-risk patients early in their hospital stay, allowing for targeted interventions (33). For example, real-time monitoring systems can alert healthcare providers to changes in vital signs or laboratory results indicative of an impending infection, facilitating timely intervention.

Education and training of healthcare staff play a pivotal role in infection prevention. Regular workshops and simulation training focused on infection control practices can enhance staff awareness and adherence to protocols (34). Additionally, patient education is crucial; empowering patients and caregivers with knowledge about the signs of infection and the importance of early reporting can lead to timely medical intervention and potentially reduce readmission rates (35).

Lastly, exploring novel therapeutic approaches such as prophylactic antibiotics in high-risk patients may warrant further investigation. While the use of prophylactic antibiotics remains controversial due to concerns about antibiotic resistance, carefully designed studies could elucidate their role in preventing infections without contributing to resistance (36).

In view of these limitations, the results of this review should be interpreted with caution because they include differences in definitions of infections.

Conclusion

Addressing infection-associated readmissions in stroke patients requires a multifaceted approach that integrates clinical care, technology, educa-

tion, and research into new preventive strategies. By adopting these comprehensive measures, we can significantly improve patient outcomes and reduce the burden of readmissions associated with infections. More rigorous studies in both high and low-income countries should be made to allow for a clear identification of clinical, patient reported, resource use as well as economic outcomes arising from the prescribing of unmedicated medicines.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflicts of Interest

The authors declare no conflict of interest.

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