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Review Article

Urinary tract infection after stroke: A narrative review

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ABSTRACT

Background: Urinary tract infection (UTI) is one of the most common infections seen in patients hospitalized for acute stroke, resulting in greater utilization of hospital resources in addition to patient discomfort. Although post-stroke infections (PSIs) are commonly referenced for interference with stroke recovery as well as associations with worse clinical outcome, factors associated specifically with UTI after stroke remain unclear.
Aim: To provide a comprehensive narrative synthesis covering literature published with results specific to the topic of UTI in stroke patients.
Methods: Literature review was performed searching the keywords "stroke" and "urinary tract infection" in Pubmed. All manuscripts published in English were appraised for information relevant to UTI in stroke patients. Applicable content was obtained, synthesized, and summarized.
Results: Post-stroke UTI is found to be associated with prolongation of hospital length of stay (LOS), discharge to a Care Home, and increased medical care costs. This process possibly reflects the consequences of greater stroke severity and clinical courses requiring urinary catheterization in hospitalized patients. However, UTI does not share an independent association with long-term clinical outcomes including morbidities and mortality.
Conclusions: A narrative review was performed, including the following topics: classifications and epidemiology, pathogenesis, clinical features, and future directions. The heterogeneous nature of reports on UTI in stroke patients remains as a major limitation in literature.

1. Introduction

It has been perceived that post-stroke infections (PSIs) interfere with patient recovery and are associated with worse outcomes [1–3]. Urinary tract infection (UTI) and pneumonia share a very similar overall incidence as the two most common PSIs [4]. However, these infections represent immensely different disease processes. A consensus that is specific to UTI within the broad category of PSIs remains unclear. Compiling the results of current and relevant literature in order to provide an inclusive representation of UTI after stroke may benefit clinicians' care. The purpose of this narrative review is to provide a comprehensive synthesis of epidemiology, pathogenesis, impact on clinical outcomes, and research direction specific to UTI in stroke patients.

2. Classifications and epidemiology

The Centers for Disease Control and Prevention (CDC) has a well-defined criterion for diagnosing and classifying UTI. Current criteria for symptomatic catheter-associated UTI (CAUTI) include the following: 1) Patient had indwelling urinary catheter in place for 2 consecutive days at the time of event; 2) Patient has experienced either fever, suprapubic tenderness, costovertebral angle pain/tenderness, increased urinary urgency, increased urinary frequency, or dysuria; and 3) Patient has a urine culture with < 3 species of bacterium cultured with at least one measuring $\geq 10^5$ colony-forming units per milliliter. Non-Catheter-associated UTI (Non-CAUTI) follows similar criteria. However, patients must either have an indwelling catheter for < 2 consecutive days or no catheterization during hospitalization [5].

UTIs may be further characterized as uncomplicated or complicated, with post-stroke UTIs typically included in the latter category. Uncomplicated UTIs are those that occur in otherwise healthy individuals, whereas a complicated UTI is a urinary infection occurring in a patient with a structural or functional abnormality of the urogenital tract. Stroke patients are typically affected by functional abnormalities such as bladder dysfunction or neurogenic bladder. Indwelling catheters and urinary retention caused by neurological disease are both considered factors associated with a compromised urinary tract, leading

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to complicated UTIs in stroke patients [11].

2.1. Overall incidence

UTIs affect between 10% and 19% of overall stroke patients and are considered one of the most common PSIs [4,7]. The findings discussed in this section suggest study design and enrollment characteristics play a role in the heterogeneity of reported UTI incidence.

The meta-analysis by Westendorp et al. from 2011 provided a solid source of baseline statistics. UTIs during the acute phase were reported in 10% of the 137,817 stroke patients [4]. Four years later, Westendorp et al. reported a 10% (127/1270 patients) incidence of UTI in the control cohort of the Preventive Antibiotics in Stroke Study (PASS), which compared the rate of infections between 1270 control stroke patients receiving standard care and 1268 treatment stroke patients with an experimental prophylactic 4-day regimen of 2 g ceftriaxone administered intravenously [6].

This estimated 10% UTI incidence in acute phase stroke patients is still commonly cited; however, epidemiological findings related to infection are subject to incongruities. A more recent meta-analysis performed by Yan et al. reported UTI in 19% of 13,513 acute stroke patients included, although 45 studies were excluded from meta-analysis for not reporting predictive factors associated with observed UTI rates [7]. Furthermore, a 2014 medical record review aiming to study infections and associated risk factors in 533 stroke patients treated under tertiary hospital care found the overall incidence of UTI to be much lower than those previously mentioned, at only 6.75% [8]. The relatively lower rates of UTI observed by Brogan et al. likely represents the influence data collection characteristics can have on results. Studies that aim to detect infection and studies that enroll patients for a longer period commonly report a higher relative incidence of UTI [4,9]. The heterogeneous nature of reporting within this field limits the usefulness of direct comparison among studies. Thus, it is important to compile the latest reports highlighting factors associated with post-stroke UTI risk.

2.2. Patient demographics

Females have higher risk of UTI independent of stroke, whereas in circumstances with more severe stroke, studies suggest male UTI incidence is comparable to that of females. Elderly and African American demographic UTI findings potentially manifest through confounders like stroke severity. Socioeconomic factors' that may be associated with post-stroke UTI are important to take into consideration. However, reports including socioeconomic status in current literature are scarce. Additional uncertainties about UTI risks arise as a consequence of incorporating UTIs into a single PSI category for analyses (Table 1).

2.2.1. Gender

Westendorp reported that UTI rates are higher in studies with a lower proportion of male patients ($p = 0.005$); with respect to populations at risk, gender was only associated with UTI as a sub-analysis excluding the 8 ICU studies ($p = 0.04$) [4]. Anatomically, this increased susceptibility is intuitive because the urethra is shorter in females than in males. In a more recent retrospective analysis of CAUTI, 300 stroke patients with indwelling catheter were matched on age, gender and admission date with non-stroke hospitalized patients with an indwelling catheter. The results indicated there was no difference in the incidence of developing CAUTI between male and female stroke patients with indwelling catheter [10]. However, some limitations are important to appreciate in this study's design; stroke severity and patient comorbidities were not included in their analysis due to a low sample of patients. Brogan et al.'s retrospective analysis shows greater proportions of UTI after stroke in females. However, these results were not significant under multivariate analysis [8]. Yan et al. found female sex to be a predisposing factor for UTI in stroke patients (odds ratio (OR) 1.93; 95% confidence interval (CI), 1.55–2.41) in their meta-analysis, although this report did not analyze catheterization or stroke as possible covariates [7]. Ultimately, these results likely reflect the higher incidence of UTIs among females, which exists in the general population [11].

Important to note, a 2017 report on ten-year temporal trends of medical complications in 575,211 intracerebral hemorrhage (ICH) patients identified from the Nationwide Inpatient Sample found that the prevalence of UTI has significantly increased in females between 2004 (18.2%) and 2013 (20.1%) ($p \leq 0.001$) with no significant change found in male ICH patients during that timeframe [12].

2.2.2. Age

Stott et al.'s prospective study on the clinical characteristics of 412 stroke patients from a single hospital determined UTI was associated with increasing age (OR 1.51; 95% CI 1.13–2.00 each decade) using multivariate binomial analysis [13]. Older mean age was observed to have a slightly higher rate of UTI after stroke without significance in Westendorp et al.'s systematic review ($p = 0.08$). However, meta-analysis supported advanced age's independent association with UTI ($p = 0.04$) using multivariate analysis of the same data [4]. Yan et al. also found older age to be a predisposing factor for UTI (OR 1.28; 95% CI 1.09–1.50) [7].

In Contrast, Brogan et al. reported the incidence of UTI increased with the age of stroke patients but without any significance in multivariate analysis including stroke severity [8]. Oddly, Stenzelius et al.'s prospective study analyzing CAUTI rates between stroke patients given two separate types of silicone catheter reported a slightly lower mean age among the total number of patients with UTI (76.8 years vs. 81.3 years; $p = 0.007$) [14]. This surprising proportion is another example of a study design's strong influence on infection rate; the study included data from two separate hospitals with different infection protocols and patients with distinctive socioeconomic profiles, which were not included in their analysis. Ultimately, the heterogeneity between study designs prevents a definitive conclusion on age and UTI in stroke patients.

2.2.3. Race

Among the studies analyzed, Otite et al.'s ten-year temporal trend in medical complications after ICH was the only one to report that African Americans had higher odds of UTI [12]. However, this trend was seen in addition to other complications like pneumonia and acute renal failure following their multivariate analysis of Nationwide Inpatient Sample data obtained between 2004 and 2013, which may reflect hospital care and health disparities seen in minority groups [12]. In general, race is not considered to be associated with UTI in stroke patients [7].

2.2.4. Socioeconomic status

Ersoz et al.'s 2007 prospective study of 110 consecutive stroke patients found no significant difference in post-stroke UTI frequencies between education level subgroups, although there was a higher incidence seen in those with lower education levels (ungraduated: 39.1% vs. primary school: 20.5% vs. secondary school: 15.0% with $p = 0.055$) [18]. Otite et al. reported no significant association between income and UTI in ICH patients. ICH patients with Medicaid had higher rates of UTI compared to patients with Medicare (OR 1.26; 95% CI 1.17–1.36), and patients with private insurance had lower odds of UTI compared to Medicare patients (OR 0.84; 95% CI 0.79–0.88), although insurance type does not always imply one's socioeconomic status [12]. The majority of studies addressing post-stroke UTI patient demographics did not analyze socioeconomic factors like income or level of education.

Table 1
Epidemiology: incidence and vulnerable populations.

Authors (year)	Methods	Patients	Relevant results
Westendorp et al. (2011)	Meta-analysis & systematic review	87 studies: 137,817 patients	- 10% incidence of UTI - ICU UTI rate 28% (no gender association) - UTI rates are higher in studies with higher stroke severity, fewer males, prospective studies, longer observational periods - Multivariate analysis results: advanced age independently associated with UTI
Westendorp et al. (2015)	Prospective randomized control trial	2550 patients	- 10% incidence of UTI in the control group
Yan et al. (2018)	Meta analysis	16 studies: 13,513 patients	- Female (OR 1.93; 95% CI, 1.55–3.41) - Age (OR 1.28; 95% CI 1.09–1.50)
Brogan et al. (2014)	Retrospective chart review	533 patients	- Incontinence was the only significant variable in multivariate analysis - Age was not a significant factor
Retelski et al. (2017)	Retrospective matched	300 catheterized patients with stroke	- No difference in the incidence of CAUTI between male and female stroke patients
Stenzelius et al. (2016)	Prospective study	380 patients	- Younger mean age among UTI stroke patients compared to non-UTI as a result of study design
Otite et al. (2016)	Prospective national inpatient sample analysis	116,706 patients with ICH	- Increasing incidence of UTI in female patients between 2004 and 2013 - Higher incidence of UTI in African Americans - No association between income and UTI - Medicaid patients have higher UTI odds versus Medicare patients (OR 1.26; 95% CI 1.17–1.36) - Patients with private insurance have lower UTI odds versus Medicare patients (OR 0.84; 95% CI 0.79–0.88)
Stott et al. (2008)	Prospective study	412 patients	- Age (OR 1.51; 95% CI 1.13–2.00 each decade)
Ersoz et al. (2007)	Prospective study	110 patients	- No association found between level of education subgroups and frequency of symptomatic UTI

3. Pathogenesis

3.1. Stroke severity and location

The reports available for inclusion suggest that a greater degree of post-stroke physical deficit plays a role in developing UTIs. However, studies have found no direct association between stroke lesion volume and UTI incidence.

Regarding stroke severity, Stott et al.'s prospective study reported that patients who developed UTI during acute stroke experienced a more disabling stroke, shown by higher hospitalization measures of modified National Institutes of Health Stroke Scale (mNIHSS) (OR 1.13; 95% CI 1.09–1.18) and higher post-stroke mRS (OR 2.57; 95% CI 1.19–3.44) [13]. Patients with a greater degree of the acute physical deficit from stroke had a higher frequency of developing UTI [4,7,13].

Among several studies addressing stroke location and size with UTI, only one provided results that separated UTI from PSIs. Urra et al.'s results suggest that larger infarct volume was significantly associated with higher incidence of pooled PSIs, but no association was found between infarct volume or admission characteristics like NIHSS and UTIs within their cohort [15]. Urra et al.'s results are from a limited number of patients. Nevertheless, this report highlights an important standard of practice for future research. Factors associated with UTI in stroke patients likely differ from those associated with other common PSIs, and therefore researching PSIs as a single category may not promote a complete understanding of individual patients' risks.

3.2. Urinary retention and catheterization

High post-void residual volume (PVR) shares an association with post-stroke UTI incidence, although the possibility this depends on stroke severity cannot be ruled out from the available studies. Catheterization is likely an independent risk factor for UTI, but timeframe of catheter placement and sanitation techniques have not been formally analyzed among post-stroke UTI reports.

Wu et al. found the majority of indwelling urinary catheterizations to be carried out within 48 hours of hospitalization among the 2803 prospectively enrolled stroke patients, with baseline stroke severity significantly associated with catheterization [16]. Among the 181 stroke patients admitted to a single inpatient rehabilitation unit in Kim et al.'s 2012 study, patients with post-void residual (PVR) > 100 ml, measurable through bladder ultrasound, had a significantly higher incidence of UTI on chi-square analysis ($p < 0.05$) [17]. Importantly, some degree of PVR occurred in both UTI and non-UTI patients and shared no significant association with UTI without the 100 ml threshold. Ersoz et al.'s 2007 study reported PVR > 50 ml as a significant factor for the frequency of UTI ($p < 0.04$) among 110 consecutive stroke patients [18]. It is important to note that neither of these associations were found using logistic regression analysis and therefore the effects of stroke severity, catheterization, and other complications should not be dismissed [17,18]. On a similar note, Brogan et al. reported urinary incontinence upon stroke admission as the only significant variable associated with UTI incidence in multivariate analysis (OR 2.96 CI 1.20, 7.35). However, patient's catheterization status and catheter timeframe were not documented [8].

Retelski et al.'s study found stroke patients had a higher rate of CAUTI compared to their matched counterpart (OR 3.53; 95% CI 1.24–10.03 p = . 018), although the limitations of this particular study have already been described in section 2.2.1 [10]. Additionally, a urinary catheter was associated with the diagnosis of UTI in Stott et al.'s prospective study of 412 acute stroke patients (OR 3.03, CI 1.41–6.52 $p < .001$) [13]. Foley catheter, in particular, has also been associated with UTI in ischemic stroke patients (OR 2.65; 95% CI 1.41–4.98) [19]. It has been reported that stroke patients are at increased risk for developing UTIs, whether catheterized or not, with nearly double the odds compared to other hospitalized groups [3]. Catheterization is a well-reported independent risk factor for UTI, as are neurological disorders, therefore it may be helpful to monitor these patients prudently during acute stroke care [3,11]. These findings have been compiled and summarized in Fig. 1, (Table 2).

Stenzelius et al. compared separate types of silicone catheters in prospectively enrolled stroke patients. Despite claims that noble metals like gold, palladium, and silver reduce bacterial adherence, which originally prompted the study design, there was no significant difference found in CAUTI incidence between the control group with silicone catheters and those given catheters coated with these noble metals [14].

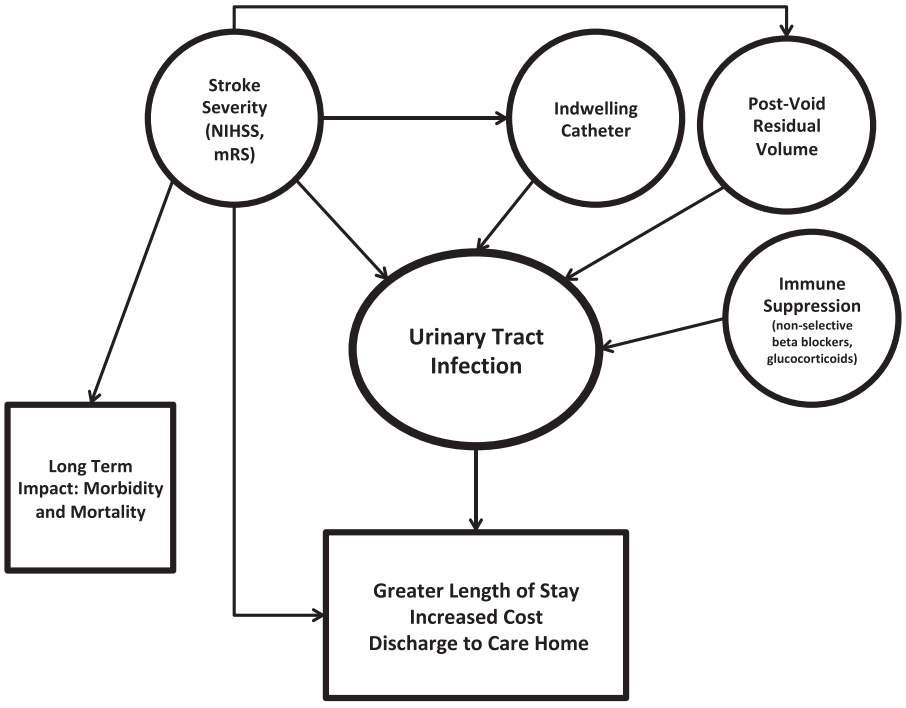

Fig. 1. Clinical features and pathogenesis of UTI in stroke patients.

3.3. Immune system after stroke

Change to the immune system is an expanding field within stroke research. Available reports on serum biomarkers, discussed below, do not currently provide insight into endogenous processes that relate to UTI specifically. Alternatively, exogenous changes caused by non-selective beta-blocker and corticosteroid treatments may influence a patient's post-stroke UTI risk.

3.3.1. Endogenous changes in immune system

Heterogenic study designs and PSI pooling have limited progress in deciphering factors associated with immunosuppression specific to UTI risk in stroke patients. For example, Wastfelt et al.'s 2018 systematic review and meta-analysis on PSIs overall concluded that there is currently a lack of studies simultaneously investigating a sufficient range of predictors for UTI, and thus, a meta-analysis was not possible [20]. Nevertheless, it is important to highlight what is known for the efficacy of study designs in the future.

Biomarkers allow clinicians to stratify the risk of infection in stroke patients; however, differentiating the risk of UTI from other infections with this method is still poorly understood. In Fluri et al.'s 2012 prospective study, 383 acute stroke patients were enrolled, they found patients' white blood cell (WBC), C-reactive protein (CRP), and procalcitonin (PCT) values on admission had a stronger prediction of UTI risk in stroke patients compared to any one of these measures independently [21]. However, the predictive value of WBC, CRP, and PCT

Table 2
Predictors of post-stroke UTI.

Author (year)	Study design	Patients characteristics	Relevant results
Fluri et al. (2012)	Prospective study on biomarkers	383 stroke patients	- Copeptin, PCT, WBC, and CRP were good predictors for the development of UTI and other PSIs, with little difference between PSIs
Urra et al. (2017)	Retrospective chart analysis	106 stroke patients	- The proportion of patients with signs of immunodepression (lymphopenia) was greater in pneumonia patients compared to UTI - Lesion volume most relevant clinical determinant of stroke-associated infection, not UTI specifically - Different PSIs differ in clinical, immunological, radiological determinants - Size and location of ischemic lesion influences pneumonia risk more than UTI
Starr et al. (2017)	Prospective cohort	1431 stroke patients	- Nonselective beta-blockade treatment associated with higher incidence of UTI on propensity score matching (13.0% vs. 5.5%, p = .009)
Retelski et al. (2017)	Retrospective matched study	300 stroke patients with indwelling catheter	- The proportion of patients who used steroids was greater among stroke patients who experienced CAUTI (55.6% vs. 24.5%)
Kim et al. (2012)	Retrospective medical record review	188 stroke patients	- UTI occurrence 4.87 times higher in patients with mean PVR > 100 ml - Stroke location, type were not associated with UTI
Brogan et al. (2014)	Retrospective Chart review	533 stroke patients	- Incontinence was the only significant variable in multivariate analysis (OR 2.96; 95% CI 1.20–7.35)
Stott et al. (2008)	Prospective cohort	412 stroke patients	- Catheterization and high mNIHSS and mRS scores during hospitalization associated with UTI - 3-month death and disability were not associated with UTI after severity, and pre-stroke disability were considered
Bogason et al. (2017)	Retrospective analysis of stroke center database	395 stroke patients	- Patients admitted from another hospital more likely to be diagnosed with a UTI (OR 2.41; 95% CI 1.18–4.95) - Foley catheter more likely to have UTI (OR 2.65; 95% CI 1.41–4.98)

on multivariable generalized estimating equations analysis also applied to pneumonia and any infection. Hence this study did not provide insight into any UTI-specific predictor among the biomarkers measured (WBC, CRP, PCT, monocytes, and copeptin) [21].

A more recent study prospectively evaluating 106 acute ischemic stroke patients for infection-associated biomarkers and neuroanatomical correlates found the proportion of patients with lymphopenia, reflecting immunodepression, was significantly greater for patients with stroke associated pneumonia (SAP) compared to patients with UTI [15]. Catheterizing patients was avoided by Urra et al., a point they highlight in consideration of the study's relatively low UTI incidence, suggesting it would be practical to evaluate immunodepression and catheterization/bladder voiding in stroke patients simultaneously in the setting of multi-centered acute stroke care.

3.3.2. Exogenous factors

The possibility that UTI is associated with iatrogenic immunosuppression arose in two studies, with beta-blockers and steroid treatments as two potential sources. Multiple studies that were initially reviewed did not specifically analyze UTI data and could not be included. The Starr et al. prospective cohort study from 2017 found a significant association between non-selective beta-blocker use and UTIs among the 1431 stroke admissions using propensity score matching (13.0% vs. 5.5%, $p = .009$) suggesting a process downstream of β2 receptor blockade may have been involved in stroke patients' UTIs [22]. Lymphocyte formation in both primary (thymus and bone marrow) and secondary (spleen, lymph nodes, and tissues) require adrenergic stimulation; in addition, virtually all immune cells aside from T(helper) type 2 cells express adrenergic receptors [23]. Although the complex immunological effects of modulating beta-adrenergic pathways are outside the scope of this review, it is important to recognize Starr et al. found no significant association between non-selective beta-blockade and either pneumonia or bacteremia among the same cohort of patients.

Retelski et al.'s retrospective study on healthcare-related variables and CAUTIs found a significantly higher proportion of CAUTIs among the stroke patients with a current prescription for steroids (prednisone, decadron, hydrocortisone, or methylprednisolone) at the time of stroke admission compared to those without (55.6% vs. 24.5%; $p = 0.004$) [10]. Glucocorticoids have well-documented immunosuppressive properties, as they are associated with anti-proliferative and apoptotic effects in immune cells in addition to raising patients' serum-glucose levels, creating an environment more favorable for infections [23].

4. Clinical features: impact of UTI on stroke outcomes

The studies discussed in this section suggest post-stroke UTI is associated with prolonged hospital stay, discharge to a care home, and increased medical cost. However, it is important to recognize UTI does not have a signficant impact on the long-term stroke outcomes based on the current evidence (Table 3).

4.1. Features and prevention of UTI

The majority of UTIs in stroke patients are hospital acquired, occurring after 48 hoursh of hospitalization [4]. Lower UTIs, including urethritis (infection of the urethra) and cystitis (infection within the bladder), are often accompanied by symptoms of dysuria (painful urination) and urinary urgency. Pyelonephritis (infection within the kidney) is described as an upper UTI and commonly includes the symptoms of a lower UTI along with flank pain, costovertebral-angle pain, nausea, vomiting, and fever [11].

Ersoz et al.'s prospective study found *Escherichia coli* to be the most common microorganism in all stroke patients, including both the subgroup of patients capable of voiding spontaneously and patients with indwelling catheters. *Pseudomonas aeruginosa* was additionally isolated in 36.4% of patients with an indwelling catheter and none of the patients without, which can be explained by *P. aeruginosa's* ability to form dense biofilms in the presence of catheters and other indwelling devices [18]. Chang et al.'s retrospective, cross-sectional comparative study including 263 acute stroke patients reported time after UTI as a contributing factor to pathogen colonization, with *Enterobacteriaceae bacilli* being the most likely pathogen found in urine culture within the first 9 days of admission and glucose-nonfermenting bacilli more likely to be present after 9 days of admission for stroke [24]. Chang et al. also reported *Acinetobacter baumanii*, *P. aeruginosa*, and other glucose nonfermenting bacilli to be unique to stroke patients, as they were not isolated in any urine cultures of 351 hospitalized coronary heart disease patients that served as a control cohort [24].

Despite reports on associations between clinical course and specific microorganism likelihood, Westendorp et al.'s PASS concluded antibiotic use for UTI prophylaxis in stroke care is not advised. Additionally, antibiotic treatment regimens are uniquely tailored to both pathogen and patient [6]. With regards to post-stroke UTI prevention, routinely monitoring PVR through portable bladder ultrasound (PBU) screening may lower the risk of UTI in stroke patients. PBU detection of PVR provides clinicians a means of confirming patients who require catheterization, preventing unnecessary catheter placements while highlighting patients with greater risk of UTI [28]. Early treatment of urinary dysfunction and early initiation of physical rehabilitation for improved ambulation and hand function in stroke patients may reduce durations of indwelling catheters, thus lowering UTI risk [18]. Generating reminders for hospitalists as to which patients presently have an indwelling catheter and requiring more experienced staff members to perform catheter placement have been reported to reduce CAUTI risk [29,30].

4.2. Short term impact

Increased length of stay (LOS) during hospitalization is a general concern. Ovbiagele et al. reported a significant difference in LOS, with a 3-day longer median time of discharge among stroke patients with a UTI [25]. Strenzelius et al.'s data also suggest patients diagnosed with UTI required an average LOS 3.5 days longer than those without UTI ($p = 0.003$) [14]. A retrospective analysis on factors associated with outcome in stroke patients during early inpatient rehabilitation found a significant increase in mean LOS with each additional complication; however, these results do not distinguish UTI patients from the 14 pooled complications [1]. The 2018 analysis from the Sentinel Stroke National Audit Program (SSNAP) reported UTI shared a slight but significant association with discharge to a Care Home (OR 1.7; 95% CI 1.04–2.75) on logistic regression modeling for risk factors among 2584 stroke patients [26].

With respect to cost, Chen et al.'s retrospective medical record analysis of 237 stroke patients reported symptomatic UTI in the rehabilitation ward to be a significant predictor related to total medical costs, measured in United States dollars (USD) under multivariate linear regression analysis (standardized coefficient = . 133, p = . 015) [27].

It is important to acknowledge that UTI's association with longer hospital stay and cost may not necessarily be a direct consequence. Bogason et al. reported no significant association between UTI and LOS or cost on multivariable analysis after stroke severity was adjusted [19]. In conclusion, stroke patients with UTI tend to require a longer hospital stay. However the possibility that both UTI and LOS is simply reflecting a more severe stroke should not be disregarded.

Two studies suggested infections, including UTI, may precede a transient increase in stroke risk [31,32]. Of these, Smeeth et al. is the only one to report a significantly greater stroke risk for patients within the first 14 days of UTI diagnosis [32]. Although these reports do not analyze risks of UTI that are specific to patients in the post-stroke acute setting, the interesting co-occurrence of UTI and stroke is worthy of mentioning.

Table 3
Impact of UTI on stroke outcomes.

Author (year)	Methods	Number of patients	Relevant results
Ovbiagele et al. (2006)	Prospective analysis of data from California Acute Stroke Prototype Registry (CASPR)	663	- UTI independently associated with greater LOS - UTI was not associated with inpatient mortality (only pneumonia)
Stenzelius et al. (2016)	Prospective study	380	- UTI patients required 3.5 days longer LOS
Janus-Laszuk et al. (2017)	Retrospective analysis	1075	- Average LOS increases with the number of complications (including UTI) - Severe disability was associated with greater number of complications
Dutta et al. (2018)	Retrospective analysis of data from the SSNAP registry	2584	- Discharge to care home associated with UTI (OR 1.70; 95% CI 1.04–2.75)
Bogason et al. (2017)	Retrospective analysis of stroke center database	395	- No significance found between UTI and mRS, LOS, hospital charges when adjusting for stroke severity
Stott et al. (2009)	Prospective	412	- UTI not associated with death or disability on binomial regression analysis adjusting for stroke severity
Wu et al. (2013)	Prospective stroke registry	2803	- UTI not associated with 3-month disability/mortality - Presence of indwelling catheter associated with 3-month disability/mortality at 3 months (OR 2.09; 95% CI 1.39–3.13)
Starr et al. (2017)	Prospective	1431	- Non-selective beta blockers may increase infection but do not change disability of mortality
Chen et al. (2016)	Retrospective medical record analysis	237	- Symptomatic UTI was a significant predictor of total medical cost under multivariate linear regression analysis

4.3. Long term impact

The importance of distinguishing UTI from the general category of PSIs becomes especially important in the discussion of long-term outcome measures after stroke hospitalization. Multiple studies suggesting PSIs are associated with worse outcome did not distinguish between the different infection processes [1,2]. Reports like these may highlight the overall importance of sanitation measures and standards of care in hospitals, but they do not help clinicians understand the specific course of post-stroke UTI.

Stott et al. reported an association between higher mRS (OR 1.79; 1.41–2.28) and death (OR 3.10; 1.69–5.69) at day 90 in stroke patients with a UTI during the acute phase per univariate analysis. However, UTI was no longer a significant predictor of combined death or disability in multivariate binomial regression analysis when adjusting for stroke severity and pre-stroke morbidity [13]. Wu et al. reported no association between UTI in stroke patients and 3-month mRS or mortality [16]. Additionally, the higher incidence of UTI seen in patients taking non-selective beta-blockers was not associated with changes in disability or mortality [22].

Despite the volume of literature suggesting PSI is associated with worse outcome, current literature suggests there is no independent association between UTI and either disability measures or death. The clinical features associated with UTI pathogenesis in stroke patients that have been synthesized through comprehensive literature review are shown in Fig. 1.

5. Conclusions and future research direction

This comprehensive literature review provides several important considerations for UTI after stroke. Stroke patients have a higher incidence of UTI compared to hospitalized individuals in general. Female's increased risk of UTI does not vanish in stroke patients, although factors related to stroke severity may mask this difference in risk profiles of males' versus females' UTI rates after stroke, as seen in the ICU setting [4]. Age may be indirectly associated with higher UTI incidence. Socioeconomic status's impact on post-stroke UTI incidence cannot be determined by available literature, representing an important future direction in stroke research. Catheterization, bladder emptying, and acute stroke impairments offer insight into assessing patient's relative risk of UTI; however, heterogeneous study designs currently prevent a more definitive answer. Additionally, patients being treated with nonselective beta-blockers or corticosteroids may require closer attention in regards to developing UTIs upon admission for stroke due to immunosuppression [10,22]. Establishing a distinct stroke unit and protocol within a hospital has been associated with subsequently lowering incidence of post-stroke UTI [33]. Future research on possible differences in post-stroke UTI characteristics between those admitted to neurology or stroke departments compared to general medicine departments may also aid in the understanding of risks.

In terms of clinical outcomes, LOS, cost, and discharge to a care home may all share an association with UTI in stroke patients [1,26,27]. However, UTI during acute stroke hospitalization is not independently associated with changes in long-term consequences like disability or mortality [13,16]. Catheter use should only be performed in cases when necessary, and measuring PVR through bladder ultrasound may hint at a higher risk for developing UTI [17,18]. Utilizing PBU as a measure for screening PVR, setting reminders, and catheter placement by experienced staff may reduce patients' post-stroke UTI risk [28–30].

Studies that report PSIs as a single category do not contribute to the assessment of individual patient's possible risks upon admission for stroke or after patients' have been diagnosed with UTI during the hospitalization. Future studies reporting and analyzing each PSI as a specific category will enhance our understanding of both the pathogenesis and clinical features associated with common PSIs, like UTI. Furthermore, multivariate analysis accounting for the severity of specific types of baseline stroke impairments is necessary to determine independent risks for UTI in hospitalized acute stroke patients.

Disclosures

The authors have no conflicts of interest to disclose.

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