

## BACKGROUND

Hospital acquired Urinary Tract Infection (UTI) is a common post-stroke complication which has been shown to have various adverse consequences (1). This includes increased odd of neurological decline during hospitalization period, worse short-term and long-term rehabilitation outcomes, as well as longer length of stay which leads to a greater financial burden.

Acute ischemic stroke has been shown to be an independent risk factor for developing UTI due to multiple factors including immunosuppression, neurogenic bladder dysfunction, and immobility. Studies have suggested that while there is an immune-mediated inflammatory response to the area of the infarct, this is followed by an overall systemic immunosuppression within a few days (2). Urinary retention is a frequently reported post-stroke complication and attributed to neurogenic bladder hyperreflexia in urodynamic studies (3). Impaired mobility and mental status increases the use of foley catheters, which is a fertile breeding ground for UTI.

Despite adverse outcomes associated with UTI, guidelines from Infectious Disease Society of America do not support treating asymptomatic UTI in the absence of objective markers of infection (4).

## OBJECTIVES

Characterize demographics and hospitalization outcomes of symptomatic (sUTI) and asymptomatic (aUTI) in stroke patients compared to a control group without infectious complication.

## METHODS

This is a retrospective cohort study based on the 2019 ischemic stroke database at the University of Kentucky. From inclusion criteria, the case group was designated as either sUTI or aUTI (Figure 1). This was then matched to a control group without evidence of infection based on age and sex.

Demographics (age, sex, and stroke mechanism based on TOAST classification) were compared using Chi-squared analysis. Outcomes included length of stay (LOS), change in pre-hospital to discharge modified Rankin Scale (delta mRS), delta NIHSS (difference between admission and discharge NIHSS), and % change in NIHSS ((highest NIHSS -lowest NIHSS)/admission NIHSS)). Mean and standard deviation between the 3 groups were compared using ANOVA.

### Inclusion criteria

- 1) Ischemic stroke
- 2) Has documented reason for obtaining urine studies
- 3) Confirmed UTI based on
  - a) Organism growth on urine culture OR
  - b) Presence of pyuria and bacteria on Urinalysis

### Exclusion Criteria

- 1) Hemorrhagic stroke
- 2) Presence of other confounding infection
- 3) Multiple UTIs that met criteria for both sUTI and aUTI during same hospitalization
- 4) Undocumented reason for obtaining urine studies

### Symptomatic UTI

### Asymptomatic UTI

- Documented subjective symptoms related to UTI (dysuria, abdominal/flank pain, increased urgency/frequency)

- Documented reason for obtaining urine studies not based on patient's subjective history or objective vital signs.

- Objective vital signs suggestive of (fever, signs of shock)

- Reasons include leukocytosis, encephalopathy, and malodorous urine.

Figure 1. Criteria for selecting UTI case group and categorizing into either sUTI or aUTI

## RESULTS

A total of 91 cases were identified as having UTI (sUTI = 34; aUTI = 57), with nearly all receiving antimicrobials (all sUTI; 96% of aUTI). Urine studies from the sUTI group was obtained due to subjective history in 59% of patients. aUTI group was primarily driven by cardioembolic mechanism (n=47%), with the overall breakdown of stroke mechanisms being distinct from the sUTI and control (Tables 1, 3). aUTI had the largest proportion of the oldest age group (>80, n=37%), and this was distinct from the sUTI group (Tables 2, 3). No difference in sex breakdown was seen (Table 3).

TOAST mechanism	Control		sUTI		aUTI	
	Patients	% distribution	Patients	% distribution	Patients	% distribution
Atheroembolic	31	34%	15	44%	7	12%
Cardioembolic	28	31%	11	32%	27	47%
Small Vessel Disease	13	14%	3	9%	11	19%
Other Etiology	8	9%	2	6%	5	9%
ESUS	11	12%	3	9%	7	12%

Table 1. Breakdown of stroke mechanism (TOAST criteria) between control, sUTI, and aUTI group.

Age	Control		sUTI		aUTI	
	Patients	% distribution	Patients	% distribution	Patients	% distribution
<59 or less	16	18%	5	15%	11	19%
60-79	50	55%	24	71%	25	44%
>80 or greater	25	27%	5	15%	21	37%

Table 2. Breakdown of age between control, sUTI, and aUTI group.

Chi Squared analysis	TOAST breakdown			Age	Sex
	Symptomatic vs. Asymptomatic UTI	Symptomatic UTI vs. Control	Asymptomatic UTI vs. Control		
		0.017	0.035	0.543	
		0.777	0.243	0.2	
		0.047	0.387	0.348	

Table 3. Chi-squared analysis of stroke mechanism, age, and sex with comparison between sUTI vs. aUTI, sUTI vs. control, and aUTI vs. control.

Both sUTI and aUTI had greater morbidity as defined by delta mRS compared to control (p=0; p=0.011 respectively), but not to each other (p=0.061). Only sUTI resulted in longer LOS compared to control and aUTI group (p=0; p=0.049 respectively). sUTI had the longest hospital length of stay and highest change in mRS scale on discharge (Figure 2, 3). No difference in delta or % change NIHSS was observed between the 3 groups (Table 4).

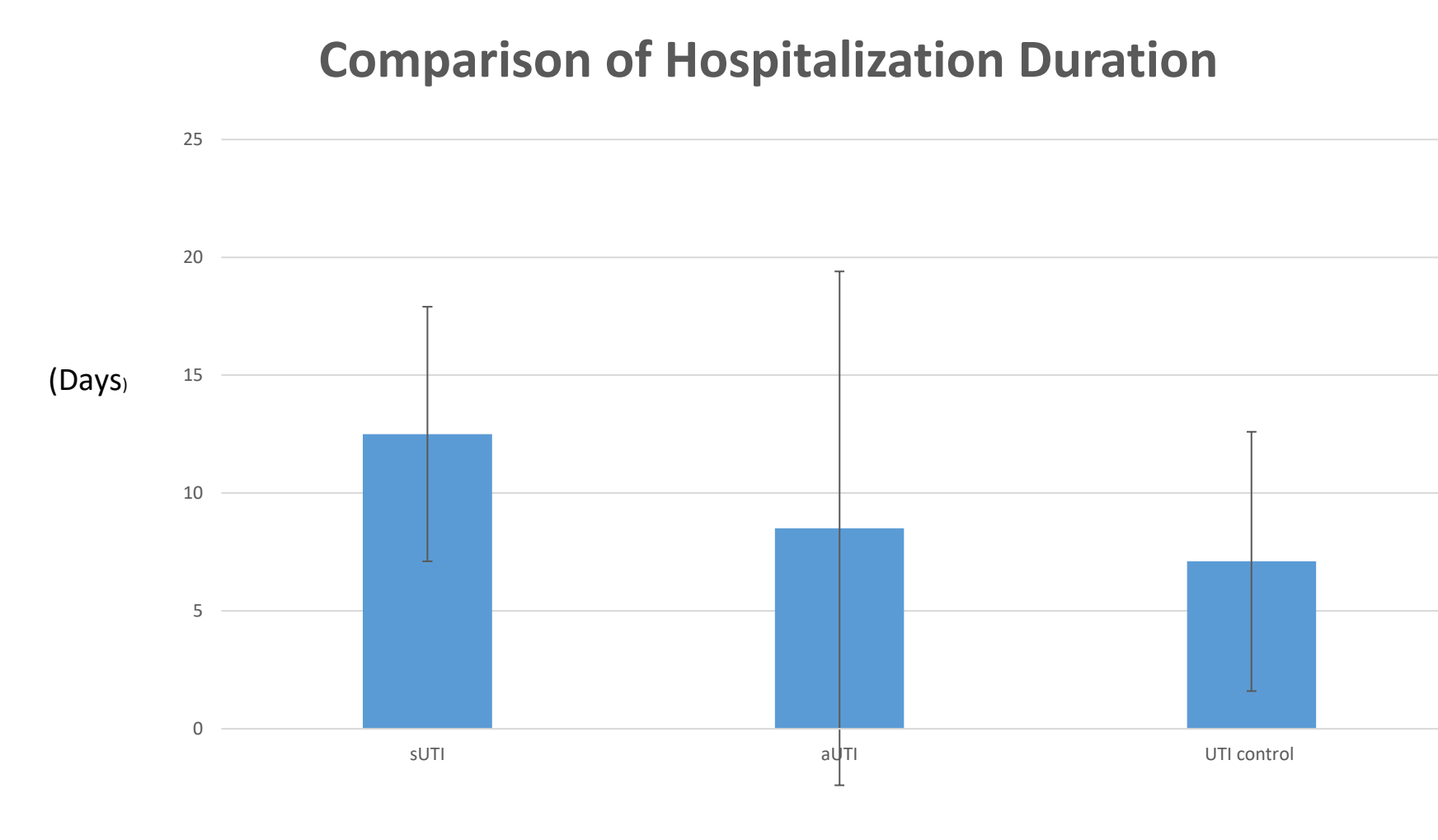


Fig 2. Comparison of hospital length of stay between sUTI, aUTI, and Control group

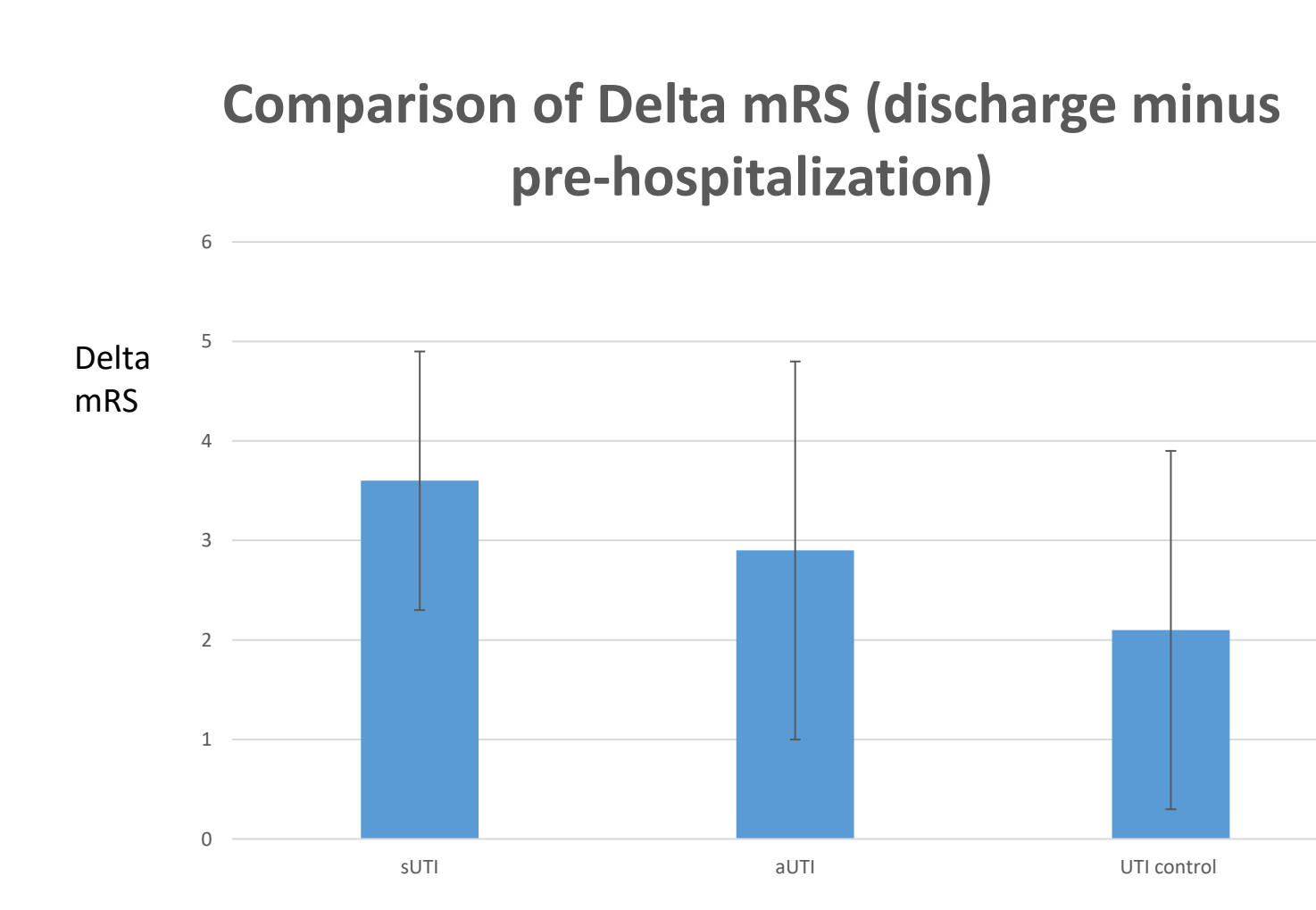


Fig 2. Comparison of Delta mRS (mRS on discharge minus pre-hospitalization) between sUTI, aUTI, and Control group

ANOVA analysis of mean	Hospital Length of stay (p)	Delta Rankin (p)	Delta NIHSS (p)	%Change in NIHSS (p)
	0.049	0.061	0.73	0.62
	0	0	0.714	0.248
	0.302	0.011	0.929	0.139

Table 4. ANOVA analysis of mean involving hospital LoS, Delta Rankin, Delta NIHSS, and % Change in NIHSS compared between sUTI, aUTI, and Control group.

## DISCUSSION

Urinary tract infection is a common infectious complication affecting up to 19% of post-stroke patients (5). It has been suggested to impair post-stroke recovery, especially during the hospitalization period, for various reasons. Biologically, UTI induces a systemic inflammatory response which has been shown to be directly detrimental to brain tissue, especially involving the ischemic penumbra (6). UTI also causes a pro-thrombotic state which has been shown to transiently increase the risk of stroke (7). Furthermore, UTI are strongly associated with use of Foley catheters and IV Antibiotics, which hamper intensive physical therapy efforts (1).

While our data did not reveal a significant change in NIHSS during hospitalization between UTI groups and control, it does suggest impairment of stroke recovery during the acute hospitalization phase based on change in mRS from admission to discharge. Both the sUTI and aUTI groups had a higher change in mRS score compared to control group, but this was not significant when compared to each other. This is consistent with prior studies showing an association with UTI and higher mRS and death at 90 days (5). Interestingly, only sUTI had a statistically significant longer hospitalization periods compared to aUTI and control. This can be explained by the fact that urine studies in this cohort was obtained due to objective evidence of infection based on vital signs in 41% of patients. Objective vital signs suggestive of infection implies that the urinary tract infection is no longer localized and is concerning for systemic sepsis.

In our demographics analysis, we found that stroke mechanism for the aUTI cohort was predominately cardioembolic and had the highest proportion of the oldest age category. There was much more even distribution between atheroembolic and cardioembolic etiology for the sUTI and control cohort as the predominant mechanism. This finding is consistent with cardioembolic strokes being the most severe subtype, both in terms of size of embolus and infarct volume (8). The territory involved in cardioembolic strokes are predominately cortical, which would manifest as aphasia and altered mental status changes (8). Aging has been shown to be a non-modifiable risk factor in terms of higher stroke severity and poor recovery outcome, thus more likely to exhibit asymptomatic UTI (9).

## CONCLUSIONS

Both sUTI and aUTI were associated with poor outcome in mRS, which may suggest impaired stroke recovery. Withholding antibiotic treatment in aUTI, as suggested by IDSA guidelines, may lead to worse outcomes. Further study is needed to determine the impact of non-treatment.

## REFERENCES

- 1) Poisson SN, Johnston SC, and Josephson SA. 2010. Urinary Tract Infections Complicating Stroke – Mechanisms, Consequences, and Possible Solutions. *Stroke*. 41 (4), 180-184.
- 2) Offner H, Vandenbark AA and, Hurn PD. 2009. Effect of experimental stroke on peripheral immunity: CNS ischemia induces profound immunosuppression. *Neuroscience*. 158: 1098-1111
- 3) Ersoz M, Tunc H, Akuz M, and Ozel S. 2005. Bladder Storage and Emptying Disorder Frequencies in Hemorrhagic and Ischemic Stroke Patients with Bladder Dysfunction. *Cerebrovasc Dis*. 20: 395-399.
- 4) Nicolle LE., Gupta K, Bradley SF, et al. 2019. Clinical Practice Guideline for the Management of Asymptomatic Bacteriuria: 2019 Update by the Infectious Disease Society of America. *Clinical Infectious Diseases*. 68(10): 75-83
- 5) Smith C, Almallouhi E, and Feng W. 2019. Urinary Tract Infection After Stroke: A Narrative Review. *Journal of the Neurological Sciences*. 403: 146-152
- 6) Welsh P, Barber M, Langhorne P, et al. 2009. Associations of Inflammatory and Haemostatic Biomarkers with Poor Outcome in Acute Ischaemic Stroke. *Cerebrovasc Dis*. 27:247-253.
- 7) Fugate JE, Lyons JL, Thakur KT, Smith BR, Hedley-Whyte ET, Mateen FJ. 2014. Infectious causes of stroke. *Lancet Infect Dis*. 14:869-80.
- 8) Arboix A and Alio J. 2010. Cardioembolic Stroke: Clinical Features, Specific Cardiac Disorders and Prognosis. *Current Cardiology Reviews*. 6: 150-161.
- 9) Roy-O'Reilly M and McCullough LD. 2018. Age and Sex are Critical Factors in Ischemic Stroke Pathology. *Endocrinology*. 159 (8): 3120-3131