Urinary Tract Infections in Hospitalized Ischemic Stroke Patients: Source and Impact on Outcome

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Abstract

Background: Urinary tract infections (UTIs) in ischemic stroke patients are a common occurrence and the frequent focus of quality improvement initiatives. However, many UTIs are community-acquired and the impact of such infections on patient outcomes remains controversial.

Methods: We conducted a retrospective analysis of our Stroke Center Database and electronic medical records to determine the incidence of both community-acquired UTI (CA-UTI) and hospital-acquired UTI (HA-UTI) in hospitalized ischemic stroke patients. We assessed risk factors for UTI, as well as clinical outcome, the length of stay (LOS), and hospital charges.

Results: In our study sample of 395 patients, UTIs were found in 11.7% and the majority of these (65%) were found on admission. Patients admitted from another hospital were more likely to be diagnosed with a UTI of any type compared to those arriving from home (odds ratio (OR) 2.42 95%, confidence interval (CI) 1.18, 4.95) and were considerably more likely to have an HA-UTI than a CA-UTI (OR 12.06 95% CI 2.14, 95.32). Those with a Foley catheter were also more likely to have a UTI (OR 2.65 95% CI 1.41, 4.98). In the multivariable analysis, we did not find a statistically significant relationship between any UTI or a specific UTI subtype and discharge modified Rankin Score (mRS), LOS, or hospital charges. Admission stroke severity remained associated with higher odds of discharge in poor condition (adjusted odds ratio (aOR) 6.23 95% CI 2.33, 16.62), an extended LOS (6.84 vs 5.07, p = 0.006), and higher hospital charges ($18,305 vs $12,162, p = 0.001).

Conclusions: Urinary tract infections remain a common occurrence in stroke patients. However, the majority of UTIs are present on admission and may have little impact on discharge clinical condition, LOS, or hospital charges. These results may have implications for quality improvement (QI) initiatives that focus on the prevention and treatment of hospital-acquired UTIs.

Introduction

Stroke is one of the leading causes of morbidity and mortality in the Western world. The care of stroke patients often requires substantial resources not only during the acute phase but also after discharge since a considerable number of patients will require constant nursing care [1]. The complication rate in stroke patients is fairly high and is linked to stroke severity, with the most common complications being falls, skin breakdown, and infections. Pneumonia and urinary tract infections (UTIs) are the most frequent types of infections seen. The incidence of infections varies, but previous studies have quoted the rate for UTI as ranging from 3% to up to 40% [2-7]. Studies have suggested a link between infection and poor clinical outcome after stroke [8]. Elimination of certain infections, including UTIs, has also been tied to changes in reimbursement [9]. For this reason, many quality improvement (QI) programs have focused on reducing the number of infections and, as part of that process, determining which infections are hospital-acquired as opposed to community-acquired. The distinction implies that hospital providers can influence the incidence of hospital-acquired infections, but not of community-acquired ones. UTI, in particular, has been a popular topic of many QI initiatives, given its relatively high frequency; yet, it also presents a challenge since many patients meet UTI criteria on admission and may have little impact on discharge clinical condition, LOS, or hospital charges. The goals of this study were to 1) access the incidence of both community and hospital-acquired UTI in our institution’s stroke population and 2) to determine what effect, if any, the presence of UTI had on various outcome measures.

Materials And Methods

We conducted a retrospective analysis of our Stroke Center Database, along with our electronic medical records to determine the incidence of both community-acquired UTI (CA-UTI) and hospital-acquired UTI (HA-UTI) in hospitalized ischemic stroke patients. We assessed risk factors for UTI, as well as clinical outcome, the length of stay (LOS), and hospital charges.
records, over a two year period. Penn State Hershey Medical Center/Penn State College of Medicine Human Subjects Protection Office (HSPO) issued approval 35304EP for this study. Patient consent was obtained or waived at the time of treatment. All patients admitted with a diagnosis of acute ischemic stroke were initially reviewed. We gathered data concerning demographic information, location of patient prior to admission (e.g., home, hospital, nursing home), Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria [10], UTI occurrence, urinalysis and urine culture results, Foley placement, presence of sepsis [11], admission and discharge modified Rankin Scores (mRS), and admission and discharge National Institutes of Health Stroke Scale (NIHSS). Admission mRS was determined based on historical information acquired from the patient, family, and medical record and reflects the condition of the patient prior to the stroke. A urinalysis (UA) was defined as positive if either nitrite or leukocyte esterase were positive. However, an actual UTI was defined as a positive urine culture. A community-acquired UTI (CA-UTI) was defined as being present on admission, while a hospital-acquired UTI (HA-UTI) was defined as being detected any time after admission. Admission and discharge NIHSS were dichotomized, with a score of > 10 being considered a severe stroke. Admission and discharge mRS were also dichotomized, with a score of three or more being considered poor condition/outcome and a score of two or less being a good baseline condition/functional outcome. The length of stay (LOS) and hospital charges were obtained from hospital records.

Statistical methods

All variables were summarized initially with frequencies and percentages or means, medians, and standard deviations. Admission and discharge mRS and NIHSS were dichotomized at the upper quartile for the sake of analysis. Logistic regression was used to determine factors that are significantly associated with any UTI versus no UTI and with hospital-acquired UTI versus community-acquired UTI. Logistic regression was also used to examine the association between poor clinical outcome and other factors. Because their distributions were skewed and not normal in nature, length of stay and hospital charges were log-transformed prior to analysis. An Analysis of Variance (ANOVA) was then used to make comparisons between the means of the groups of other variables. The means and confidence limits resulting from the ANOVA were exponentiated back to their original units. Tukey’s method was used to adjust for multiple comparisons for variables with more than two groups. A multivariable model was applied to each outcome that included all variables from the bivariate analysis. The odds ratios and mean estimates from the multivariable models were adjusted for all other variables in the model. Multicollinearity was tested for between variables using variance inflation factors (VIF) statistics from linear regression, but none were found. The fit of the logistic regression model was checked using Deviance, Pearson, and Hosmer and Lemeshow goodness-of-fit statistics. All analyses were performed using SAS® 9.4 (SAS Institute, Cary, NC).

Results

The initial review yielded 404 observations, but after limiting this to unique subjects based on the last admission date, we were left with 395 patients. The demographic information for the included patients can be seen in Table 1.
Urinary catheters were placed in 122 patients (33%) with the majority placed at our institution. The total UTI occurrence was 11.7%, with the majority of UTIs (65%) being present on admission. The mRS on admission was considered good (≤ 2) for 311 patients (78%) while, on discharge, the mRS was good for 268 patients (68%).

Results of a bivariate logistic regression for factors associated with UTI, or with CA-UTI versus HA-UTI in our study population, can be seen in Table 2.

### TABLE 1: Overall Patient Characteristics

mRS: modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale; SD: standard deviation; TOAST: Trial of Org 10172 in Acute Stroke Treatment; UA - urinalysis; WBC: white blood count

| Variable (N = 395) | N (%) or Mean ± SD |
|--------------------|--------------------|
| Age (years)        | 68.5 ± 16.6        |
| Female             | 182 (46.1)         |
| Urinary tract infection | 30 (7.6) |
| Community-acquired | 16 (4.1)           |
| Hospital-acquired  | 349 (88.4)         |
| None               |                    |
| Admission source   |                    |
| Home               | 289 (73.2)         |
| Outside hospital   | 81 (20.5)          |
| Nursing home       | 25 (6.3)           |
| Foley              | 122 (33.0)         |
| UA positive results| 52 (16.9)          |
| UA positive nitrites| 36 (12.8)         |
| UA positive leukocytes | 75 (26.5)  |
| UA positive bacteria| 185 (76.8)       |
| UA positive sepsis | 19 (4.8)           |
| UA WBC in urine > 4| 71 (18.0)          |
| TOAST criteria     | 113 (28.6)         |
| Large vessel       | 102 (25.8)         |
| Small vessel       | 88 (22.3)          |
| CardioEmbolic      | 65 (16.5)          |
| Other determined   | 27 (6.8)           |
| Admission severe stroke (NIHSS ≥ 10) | 79 (21.0) |
| Admission poor condition (mRS ≥ 3) | 84 (22.3) |
| Discharge severe stroke (NIHSS ≥ 10) | 61 (16.1) |
| Discharge poor condition (mRS ≥ 3) | 127 (32.2) |
| Length of stay (days) | 5.47 ± 4.10 |
| Hospital charges ($) | 13,660 ± 11,747  |
**TABLE 2: Factors Associated with UTI Overall or with Hospital-acquired UTI Versus UTI on Admission**

* Odds ratios and p-values from logistic regression, exact logistic regression used if needed.

mRS: modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale; TOAST: Trial of Org 10172 in Acute Stroke Treatment; UA: urinalysis; UTI: urinary tract infection
Patients admitted from another hospital were more likely to be diagnosed with a UTI compared to those arriving from home (OR 2.42 95% CI 1.18, 4.95). Similarly, those with a Foley catheter were also more likely to be diagnosed with a UTI (OR 2.65 95% CI 1.41, 4.98). As expected, since it is one of the diagnostic tests for UTI, positive UA results were strongly associated with the diagnosis of UTI (as defined as a positive urine culture). Stroke severity (admission NIHSS) and preadmission condition (preadmission mRS) were not associated with UTI. When comparing CA-UTI versus HA-UTI, those patients admitted from an outside hospital were considerably more likely to develop an HA-UTI than a CA-UTI (OR 12.06 95% CI 2.14, 95.32). For patients admitted from a nursing home the finding, although not statistically significant, was reversed. Patients in the highest age quartile (> 81) were significantly less likely to suffer from a HA-UTI as opposed to a CA-UTI (OR 0.04 95% CI 0.0, 0.62). Stroke severity and preadmission condition (as defined by preadmission mRS) were not significantly associated with either CA-UTI or HA-UTI.

A bivariate analysis of the factors associated with the clinical condition on discharge, the length of stay, and hospital charges can be seen in Table 3.

| Variable                        | Discharge Poor Condition † | Length of Stay (days) ‡ | Hospital Charges ($) ‡ |
|---------------------------------|-----------------------------|-------------------------|-------------------------|
| (N = 395)                       | (N = 373)                   | (N = 373)               |                          |
| N (%)                           | OR (95% CI)                 | Mean (95% CI) Differences | Mean (95% CI) Differences |
| Any UTI                         |                             |                         |                          |
| Yes                             | 19 (41.3)                   | 1.57 (0.84, 2.96)       | 5.51 (4.51, 6.73)        | Yes > No                  | 13100 (10864, 15768) |
| No                              | 108 (31.0)                  | Reference               | 4.18 (3.88, 4.51)        |                          | 10523 (9817, 11281) |
| UTI Type                        |                             |                         |                          |
| None                            | 108 (31.0)                  | Reference               | 4.18 (3.88, 4.50)        | Hosp > Comm               | 10523 (9820, 11277) |
| Hospital-acquired               | 6 (17.5)                    | 1.33 (0.48, 3.78)       | 8.08 (5.78, 11.31)       | Hosp > None               | 17354 (12694, 23725) |
| Community-acquired              | 13 (43.3)                   | 1.71 (0.80, 3.64)       | 4.49 (3.51, 5.74)        |                          | 11276 (8974, 14169) |
| Age (years)                     |                             |                         |                          |
| Q1: ≤ 58                        | 29 (28.2)                   | Reference               | 4.50 (3.91, 5.18)        |                          | 12414 (10912, 14124) |
| Q2: 59-72                       | 32 (31.7)                   | 1.18 (0.65, 2.16)       | 4.22 (3.67, 4.85)        |                          | 10738 (9451, 12201) |
| Q3: 73-81                       | 23 (24.2)                   | 0.82 (0.43, 1.54)       | 4.23 (3.66, 4.89)        |                          | 10143 (8883, 11581) |
| Q4: > 81                        | 43 (44.8)                   | 2.07 (1.15, 3.73)       | 4.37 (3.78, 5.04)        |                          | 10041 (8801, 11456) |
| Gender                          |                             |                         |                          |
| Female                          | 57 (31.3)                   | 0.93 (0.61, 1.42)       | 4.68 (4.22, 5.18)        | Female > Male            | 11173 (10161, 12298) |
| Male                            | 70 (32.9)                   | Reference               | 4.03 (3.66, 4.44)        |                          | 10495 (8589, 11486) |
| Admission Source                |                             |                         |                          |
| Home                            | 74 (25.6)                   | Reference               | 3.92 (3.62, 4.25)        |                          | 9620 (9113, 10562) |
| Outside hospital (OSH)          | 34 (42.0)                   | 2.10 (1.26, 3.52)       | 5.69 (4.91, 6.61)        | OSH > Home               | 13005 (10136, 16919) |
| Nursing home                    | 19 (76.0)                   | 9.20 (3.54, 23.91)      | 5.29 (4.01, 6.51)        |                          | 14156 (12339, 16331) |
As expected, older age, a more severe stroke and a poor condition on admission were all associated with higher odds of a poor outcome. However, while the presence of a Foley catheter was also associated with a poor outcome, the presence of a UTI itself was not. The presence of a UTI of any type was associated with an increased LOS and increased hospital charges. Patients with a HA-UTI had a longer length of stay than both CA-UTI patients and those patients without a UTI of any type. Again, illness severity in terms of preadmission mRS and admission NIHSS were associated with longer LOS and greater hospital charges.

Finally, Table 4 shows the results of a multivariate analysis of factors associated with clinical outcome, LOS, and hospital charges while adjusting for all other co-factors.

## TABLE 3: Factors Associated with Poor Clinical Outcome, Length of Stay, and Hospital Charges

| Factor                              | Yes (76.0) | 13.89 (7.68, 25.15) | 6.62 (5.72, 7.66) | 6.62 (5.72, 7.66) | 17862 (15726, 20288) | Yes > No | Yes > No |
|-------------------------------------|------------|---------------------|-------------------|-------------------|----------------------|----------|----------|
| Admission severe stroke (NIHSS ≥ 10)| Yes        | 60 (76.0)           | 13.89 (7.68, 25.15) | 6.62 (5.72, 7.66) | 17862 (15726, 20288) | Yes > No | Yes > No |
|                                     | No         | 55 (18.5)           | Reference         | 3.78 (3.50, 4.08) | 9251 (8646, 9898)    |          |          |
| Admission poor condition (mRS ≥ 3)  | Yes        | 58 (69.1)           | 9.61 (5.56, 16.62) | 5.42 (4.67, 6.30) | 13508 (11770, 15503) | Yes > No | Yes > No |
|                                     | No         | 55 (18.8)           | Reference         | 3.98 (3.66, 4.31) | 10011 (9288, 10789)  |          |          |

† Odds ratios and p-values from logistic regression, odds ratios adjusted for all other variables in the table
‡ Means, 95% confidence limits, and pairwise comparisons from Analysis of Variance (ANOVA), means adjusted for all other variables in the table

mRS: modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale; TOAST: Trial of Org 10172 in Acute Stroke Treatment; UA - urinalysis; UTI: urinary tract infection
| Variable                        | Discharge Poor Condition † | Length of Stay (days) ‡ | Hospital Charges ($) ‡ | N (%) | OR (95% CI) | Differences | Mean (95% CI) | Differences |
|--------------------------------|-----------------------------|-------------------------|------------------------|-------|-------------|-------------|---------------|-------------|
|                                | (N = 247)                  | (N = 232)               | (N = 232)              |       |             |             |               |             |
| Any UTI*                       |                             |                         |                        |       |             |             |               |             |
| Yes                            | 15 (37.5)                  | 0.51 (0.14, 1.89)       | 5.58 (4.36, 7.14)      | 14526 (11843, 17817) |
| No                             | 65 (31.4)                  | Reference               | 5.50 (4.45, 6.80)      | 14910 (12514, 17763) |
| UTI Type                       |                             |                         |                        |       |             |             |               |             |
| None                           | 65 (31.4)                  | Reference               | 5.60 (4.53, 6.92)      | 14989 (12567, 17878) |
| Hospital-acquired              | 4 (30.8)                   | 0.48 (0.08, 2.91)       | 7.31 (4.83, 11.07)     | 15805 (11200, 22304) |
| Community-acquired             | 11 (40.7)                  | 0.53 (0.12, 2.35)       | 4.98 (3.75, 6.61)      | 14021 (11082, 17740) |
| Age (years)                    |                             |                         |                        |       |             |             |               |             |
| Q1: ≤ 58                       | 20 (29.4)                  | Reference               | 6.27 (4.87, 8.07)      | 16911 (13715, 20852) |
| Q2: 59-72                      | 14 (25.0)                  | 1.08 (0.36, 3.24)       | 5.83 (4.54, 7.50)      | 15526 (12604, 19127) |
| Q3: 73-81                      | 15 (23.8)                  | 1.01 (0.36, 2.84)       | 5.54 (4.30, 7.15)      | 13694 (11085, 16919) |
| Q4: > 81                       | 31 (51.7)                  | 2.61 (0.85, 8.00)       | 5.92 (4.67, 7.51)      | 13783 (11310, 16797) |
| Gender                         |                             |                         |                        |       |             |             |               |             |
| Female                         | 41 (33.3)                  | 0.67 (0.30, 1.50)       | 6.28 (5.14, 7.67)      | 14814 (12551, 17484) |
| Male                           | 39 (31.5)                  | Reference               | 5.52 (4.39, 6.93)      | 15028 (12434, 18163) |
| Admission Source               |                             |                         |                        |       |             |             |               |             |
| Home                           | 47 (27.2)                  | Reference               | 5.66 (4.57, 7.02)      | 14753 (12347, 17627) |
| Outside hospital               | 21 (36.8)                  | 2.21 (0.34, 14.54)      | 6.30 (5.05, 7.85)      | 14616 (12169, 17555) |
| Nursing home                   | 12 (70.6)                  | 0.73 (0.28, 1.93)       | 5.72 (3.90, 8.37)      | 15405 (11224, 21143) |
| Foley                          |                             |                         |                        |       |             |             |               |             |
| Yes                            | 52 (56.5)                  | 2.34 (1.02, 5.36)       | 6.73 (5.49, 8.24)      | 17962 (15175, 21260) |
| No                             | 28 (18.1)                  | Reference               | 5.15 (4.07, 6.52)      | P = 0.014 12394 (10186, 15081) |
| UA positive results            |                             |                         |                        |       |             |             |               |             |
| Positive                       | 19 (41.3)                  | 3.13 (0.96, 10.20)      | 6.42 (5.00, 8.24)      | 16258 (13211, 20007) |
| Negative                       | 61 (30.4)                  | Reference               | 5.39 (4.22, 6.89)      | 13693 (11176, 16778) |
### TABLE 4: Factors Associated with Poor Clinical Outcome, Length of Stay, and Hospital Charges Adjusted for All Other Factors

* Any UTI is adjusted for all variables included the table but the estimates for the other variables are from the model including UTI type

† Odds ratios and p-values from logistic regression, odds ratios adjusted for all other variables in the table

‡ Means, 95% confidence limits, and pairwise comparisons from Analysis of Variance (ANOVA), means adjusted for all other variables in the table

mRS: modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale; TOAST: Trial of Org 10172 in Acute Stroke Treatment; UA - urinalysis; UTI: urinary tract infection

Two separate statistical models were used. In the first, any UTI was modeled with the other covariates (first row), while in the second, UTI type (none, CA-UTI, or HA-UTI) was modeled (all other rows include results from this model). After adjusting for the various covariates, we did not find a statistically significant relationship between either any UTI or a specific UTI subtype and discharge mRS, LOS, or hospital charges. However, the presence of a Foley catheter was associated with poor clinical outcome (adjusted odds ratio (aOR) 2.34 95% CI 1.02, 5.36), increased LOS (6.73 days versus 5.15 days, p = 0.04), and increased hospital charges ($17,962 versus $12,394, p < 0.001). Admission stroke severity remained associated with higher odds of discharge in poor condition (aOR 6.23 95% CI 2.33, 16.62), a longer number of days LOS (6.84 versus 5.07, p = 0.017) and higher hospital charges ($18,305 vs $12,162, p < 0.001).

**Discussion**

The role of infection in ischemic stroke is likely to be complex and multifactorial. Infection may play a causal role in the immunological triggering of stroke, and a stroke itself may have untoward effects on the immune system. Syrjänen, et al. found increased serum bacterial antibody levels in young patients with acute stroke compared to controls [12]. Subsequent papers also reported that infection is a risk factor for stroke with up to 25-35% of stroke patients having infections preceding their stroke [13-14]. The concepts of central nervous system (CNS) injury-induced immunodepression or stroke-induced immunodepression have even been used to describe the findings of secondary immunodeficiency after stroke [15-16]. While therapeutic immunomodulation as a treatment for stroke has not resulted in clear outcome improvement in humans, at least one study focusing on prophylactic antibiotic therapy for acute stroke yielded promising results [17]. UTI, in particular, is one of the most common infections seen in stroke patients. In addition, unlike other infections such as pneumonia or invasive line infections, UTI are often present on admission,
which complicates efforts at eradication. Given its frequency, it is therefore not surprising that detection of CA-UTI and a reduction in HA-UTI have been the focus of numerous QI initiatives. However, it is not clear that the early detection and treatment of a CA-UTI or the later finding of a HA-UTI by themselves portend a poor outcome. Rather, since many UTIs are minimally symptomatic and, in general, are easily and inexpensive treated, the overall impact on a complex disease, such as stroke, may be minimal.

In an effort to better understand the role the diagnosis of UTI plays in the course of an ischemic stroke patient, we examined the incidence and implications of a UTI diagnosis on all of the ischemic stroke patients admitted to a single institution over a two-year period. We defined a UTI as a positive urine culture since our practice is to treat with antibiotics only those patients that have a positive culture. Data collected included the frequency of urinary catheter placement, UA results, and clinical outcome at discharge, as well as information on length of stay (LOS) and hospital charges. The rate of UTI in our population was approximately 12% with majority (65%) being found on admission (CA-UTI). Previous studies in stroke patients have quoted a wide range of rates for UTI, from as low as 3% up to as high as 44% [18]. Much of this variability can be explained by the length of follow-up, with a higher rate of UTI found in populations with longer follow-up periods. In addition, our HA-UTI rate was 4.1%, considerably lower than that reported in two older studies from 2000 and 2009 (16% and 24%) [5, 19]. It is possible that this reduction in the HA-UTI rate may be due to QI initiatives launched over the past few years, but unfortunately, robust data from earlier years is not available.

In our analysis, older patients were more likely to be found to have a UTI. In the oldest age group (> 81 years of age), patients were also significantly more likely to have come from a nursing home. This association can be explained by the fact that patients in nursing homes tend to have a higher incidence of infections, such as UTI, as well as being older with more comorbidities compared to patients residing at home [20]. It should be noted that although older people may be more likely to get a HA-UTI, they are also more likely to have a CA-UTI; in this study design, patients cannot crossover from a CA-UTI to a HA-UTI. For the TOAST criteria subcategories, large vessel, cardioembolic, and other determined had a higher incidence of poor mRS. These findings correlate with previous studies that have shown a worse outcome with these categories compared to others, such as a small vessel [21-23]. Urinary catheters were also a risk factor for UTI, as has been studied extensively [24]. As expected, overall UA results were associated with UTI as defined as a positive urine culture.

While overall rates of UTIs, CA-UTIs, and HA-UTIs were relatively low, we were most interested in whether these infections had any impact on the outcome. To assess clinical outcome, we chose to use the patient’s clinical status (mRS) at discharge, since we felt that this earlier time point would be more likely to be impacted by an event during the patient’s hospital course and that patients themselves would be most interested in their functional status. We included LOS and hospital charges as these parameters are frequently used as benchmarks in QI initiatives. Confirming the representativeness of our stroke population, our multivariable analysis found that stroke severity and preadmission clinical condition were strongly correlated with the clinical condition at discharge. As expected, patients with more severe strokes also had longer hospital stays and generated more hospital charges. However, importantly, this same analysis did not find a statistically significant association between UTI in general or a specific type of UTI (CA-UTI vs HA-UTI) and any of the three outcome measures studied. This finding does not mean that it should be concluded that UTI in stroke patients should not be treated, rather this finding suggests that QI efforts to eradicate UTI should be viewed realistically in terms of their overall impact on the stroke patient. It would appear that even if expensive and time-consuming QI efforts are successful in eliminating HA-UTI, such efforts would be unlikely to improve the clinical outcome of stroke patients and may not produce a substantial cost saving for the healthcare facility either. In the end, UTI may be a small piece of the overall picture in the recovery of the complicated stroke patient.

Obviously, this may be a controversial assertion and previous reports have shown conflicting results regarding the impact of UTI on stroke patients. While some studies have found a correlation between UTIs and poor outcome [4, 25], others have not [19]. A study by Tirschwell, et al. [26] found a 40% increase in the length of stay in stroke patients with UTI. However, although age and gender were controlled for, stroke severity was not. In addition, CA-UTI and HA-UTI were not separately assessed. Aslanyan, et al. [4] showed an association after multivariate analysis of UTI and poor outcome by mRS at three months, but again, this study did not distinguish between CA-UTI and HA-UTI. On the other hand, an initial association of UTI with death and disability found by Stott, et al. [19] on univariate analysis failed to remain significant after controlling for stroke severity and pre-stroke morbidity. To our knowledge, this is the first study to examine the impact of UTI on mRS, the length of stay, and hospital charges in stroke patients while simultaneously differentiating between CA-UTI versus HA-UTI.

The limitations of this study, as with other studies that have looked at this subject, include the inherent problems and biases of a retrospective design. Since follow-up is limited to hospital discharge, it is possible that there may have been a delayed effect of UTI on the outcome, although this would seem to be unlikely as most stroke patients who survive their initial hospitalization tend to improve. It is also possible that the sample size was too small to detect a statistically significant difference. However, the finding that during two years at a reasonably busy Joint Commission-certified Primary Stroke Center, the occurrence of a UTI of any type had no independent impact on clinical outcome remains clinically relevant. In terms of the
outcome measures, it may be argued that the mRS is not sensitive enough; however, for the patient, the presence or absence of disability is vitally important. The length of stay and hospital charges may have varying relevance to the patient, but they are commonly used as metrics to assess the impact of QI programs.

Conclusions
Urinary tract infections remain a common occurrence in stroke patients. In our study, the majority of UTIs were present on admission, which makes admission screening an important component of any hospital QI program where UTIs are concerned. However, after adjusting for stroke severity and preadmission condition, we did not find a significant association between UTI of any type and early clinical condition, the length of stay, or hospital charges. These results suggest that QI initiatives focusing on the prevention and treatment of hospital-acquired UTIs may have minimal impact on traditional outcome benchmarks.

Additional Information
Disclosures
Human subjects: Consent was obtained by all participants in this study. Penn State Hershey Medical Center / Penn State College of Medicine / Human Subjects Protection Office (HISPO) issued approval 35304EP.
Animal subjects: All authors have confirmed that this study did not involve animal subjects or tissue.
Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References
1. Lloyd-Jones D, Adams R, Carnethon M, De Simone G, Fergusson TB, Flegal K, Ford E, Furie K, Go A, Greenland K, Haase N, Hailpern S, Ho M, Howard V, Kissela B, Kittner S, Lackland D, Lisabeth L, Marelli A, McDermott M, Meigs J, Mozaffarian D, Nichol G, O’Donnell C, Roger V, Rosamond W, Sacco R, Sorlie P, Stafford R, Steinberger J, Thom T, Wassef-Martel-Smieller S, Wong N, Wylie-Rosett J, Hong Y; American Heart Association Statistics Committee and Stroke Statistics Subcommittee: Heart disease and stroke statistics: 2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2009, 119:480–486. 10.1161/CIRCULATIONAHA.108.191259
2. Davenport RJ, Dennis MS, Wellwood I, Warlow CP: Complications after acute stroke. Stroke. 1996, 27:415-20. 10.1161/01.STR.27.3.415
3. Erozs M, Ulasyo H, Oktar MA, Akyuz M: Urinary tract infection and bacteriuria in stroke patients: frequencies, pathogen microorganisms, and risk factors. Am J Phys Med Rehabil. 2007, 86:734–41. 10.1097/PHM.0b013e31813e599b
4. Aslanyan S, Weir CJ, Diener HC, Kaste M, Lees KR; GAIN International Steering Committee and Investigators: Pneumonia and urinary tract infection after acute ischaemic stroke: a tertiary analysis of the GAIN International trial. Eur J Neurol. 2004, 11:49–53. 10.1111/j.1468-1331.2003.00749.x
5. Langhorne P, Stott DJ, Robertson I, MacDonald J, Jones L, McAlpine C, Dick F, Taylor GS, Murray G: Medical complications after stroke: a multicenter study. Stroke. 2000, 31:1225-29. 10.1161/01.STR.31.12.1225
6. McLean D: Medical complications experienced by a cohort of stroke survivors during inpatient, tertiary-level stroke rehabilitation. Arch Phys Med Rehabil. 2004, 85:466–69. 10.1016/j.ajpmr.2003.07.048-2
7. Hamidob NN, Raymond AA, Norilnah MI, Jefferel RB: The predictors of early infection after an acute ischaemic stroke. Singapore Med J. 2005, 44:544–46.
8. Boehme AK, Kumar AD, Dorsey AM, Siegler JE, Aswani MS, Leyerly MJ, Monlezun DJ, George AJ, Albright KC, Beasley TM, Martin-Schild S: Infections present on admission compared with hospital-acquired infections in acute ischemic stroke patients. J Stroke Cerebrovasc Dis. 2015, 22:e582–89. Accessed: 8/15/2015: http://www.strokejournal.org/article/S1052-3057(15)00286-5/abstract. 10.1016/j.jstrokecerebrovasdis.2015.07.020
9. Centers for Medicare and Medicaid Services (CMS), HHS: Medicare program: changes to the hospital inpatient prospective payment systems and fiscal year 2009 rates; payments for graduate medical education in certain emergency situations; changes to disclosure of physician ownership in hospitals and physician self-referral rules; updates to the long-term care prospective payment system; updates to certain IPPS-excluded hospitals; and collection of information regarding financial relationships between hospitals. Final rules. Fed Regist. 2008, 73:48435–9084.
10. Adams HP Jr, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, Marsh EE 3rd: Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke. 1995, 24:35-45. 10.1161/01.STR.24.1.35
11. ACCP/SCCM Consensus Conference Committee: American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Crit Care Med. 1992, 20:864–74.
12. Syrjanen J, Valtonen VV, Ivinnen M, Hovi T, Makkamäki M, Mäkelä PH: Association between cerebral infarction and increased serum bacterial antibody levels in young adults. Acta Neurol Scand. 1986, 75:273–78. 10.1111/j.1600-0404.1986.tb03275.x
13. Syrjanen J, Valtonen VV, Ivinnen M, Kaste M, Huttunen JK: Preceding infection as an important risk factor for ischaemic brain infarction in young and middle aged patients. Br Med J (Clin Res Ed). 1988,
296:1156–60. 10.1136/bmj.296.6630.1156

14. Paganini-Hill A, Lozano E, Fischberg G, Perez Barreto M, Rajamani K, Ameriso SF, Heseltine PN, Fisher M: Infection and risk of ischemic stroke: differences among stroke subtypes. Stroke. 2005, 34:452–57. 10.1161/01.STR.0000154112.28410.99

15. Meisel C, Schwab JM, Prass K, Meisel A, Dirnagl U: Central nervous system injury-induced immune deficiency syndrome. Nat Rev Neurosci. 2005, 6:775–86. 10.1038/nrn1765

16. Dirnagl U, Klehm J, Braun J, Harms H, Meisel C, Ziemssen T, Prass K, Meisel A: Stroke-induced immunodepression: experimental evidence and clinical relevance. Stroke. 2007, 38:770–75. 10.1161/01.STR.0000251441.89665.bc

17. Schwarz S, Al-Shailawi F, Sick C, Meairs S, Hennerici MG: Effects of prophylactic antibiotic therapy with mezlocillin plus sulbactam on the incidence and height of fever after severe acute ischemic stroke: the Mannheim infection in stroke study (MISS). Stroke. 2008, 39:1220–25. 10.1161/STROKEAHA.107.499533

18. Dromerick A, Reding M: Medical and neurological complications during inpatient stroke rehabilitation. Stroke. 1994, 25:358–61. 10.1161/01.STR.25.2.358

19. Stott DJ, Falconer A, Miller H, Tilston JC, Langhorne P: Urinary tract infection after stroke. QJM. 2009, 102:243–49. 10.1093/qjmed/hcp012

20. Nicolle LE; SHEA Long-Term-Care Committee: Urinary tract infections in long-term care facilities. Infect Control Hosp Epidemiol. 2001, 22:167–75. 10.1086/501886

21. Patel A, Mauwala Z, Limaye K, Blanchi N, Hinduja A, Patel R: Compare the functional outcome in ischemic strokes based on the TOAST classification. Neurology. 2014, 82:P1–117.

22. Liu X, Xu G, Wu W, Zhang R, Yin Q, Zhu W: Subtypes and one-year survival of first-ever stroke in Chinese patients: The Nanjing Stroke Registry. Cerebrovasc Dis. 2006, 22:130–36. 10.1159/000095241

23. Kolominsky-Rabas PL, Weber M, Geffier O, Neundoerfer B, Heuschmann PU: Epidemiology of ischemic stroke subtypes according to TOAST criteria: incidence, recurrence, and long-term survival in ischemic stroke subtypes: a population-based study. Stroke. 2001, 32:2735-40. 10.1161/ha1201.100209

24. Gould CV, Umscheid CA, Agarwal RK, Kunz T, Pegues DA; Healthcare Infection Control Practices Advisory Committee: Guideline for prevention of catheter-associated urinary tract infections 2009. Infect Control Hosp Epidemiol. 2010, 31:519–26. 10.1086/501994700000590X

25. Ifejika-Jones NL, Peng H, Noser EA, Francisco GE, Grotta JC: Hospital-acquired symptomatic urinary tract infection in patients admitted to an academic stroke center affects discharge disposition. PM R. 2015, 5:9–15. 10.1016/j.pmr.2012.08.002

26. Tirschwell DL, Kukull WA, Longstreth WT Jr: Medical complications of ischemic stroke and length of hospital stay: experience in Seattle, Washington. J Stroke Cerebrovasc Dis. 1999, 8:356–63. 10.1016/S1052-5575(99)80008-1