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Urinary tract infection after stroke

D.J. STOTT, A. FALCONER, H. MILLER, J.C. TILSTON and P. LANGHORNE

From the Academic Section of Geriatric Medicine, University of Glasgow, Faculty of Medicine, Glasgow Royal Infirmary, Glasgow G31 2ER, UK

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Summary

Background: Urinary tract infection (UTI) is a recognized complication of stroke. We aimed to determine the incidence of UTI after acute stroke, the risk factors associated with this complication, and its association with outcome.

Methods: Prospective study of consecutive acute stroke patients admitted to an urban teaching hospital. Routine clinical assessment included the modified National Institutes of Health Stroke Scale (mNIHSS) and modified Rankin scale (mRS). Patients were followed up for 3 months, including recording of clinician diagnosis of UTI.

Results: We studied 412 patients; 65 (15.8%) were diagnosed with UTI, at a median of 14 days (IQR = 4–39) post-stroke. In a binomial multivariate regression analysis, UTI was associated with urinary catheterization (OR = 3.03, 95% CI 1.41–6.52), higher mRS (OR = 1.85, 1.29–2.64) and increasing age (OR = 1.51, 1.13–2.00 for each decade). UTI was associated with death or disability at 3 months, however, this link was attenuated and became non-significant when measures of stroke severity and pre-stroke morbidity were included in a multivariate analysis.

Conclusions: UTI is common after acute stroke. It is associated with urinary catheterization, post-stroke disability and increasing age. Avoidance of catheterization might reduce the incidence of this common complication.

Introduction

Urinary tract infection (UTI) is thought to be a common complication of stroke. Previous studies have found a highly variable incidence of between 3% and 44%.[1–19] Factors claimed to predict increased risk of UTI include stroke severity,[4,18] depressed conscious level[16] increased post-void residual urine volume[20] and diabetes mellitus.[13] However, many of the studies of post-stroke UTI have limitations, including short follow-up,[16,17] retrospective design,[19,21] small sample size[3,9,16,17,19–21] or a highly selected and therefore potentially unrepresentative cohort such as participants in a randomized controlled trial[4] or subjects entering a specialist rehabilitation facility.[3,9,11,14,19–21]

UTI is associated with morbidity and as a consequence may interfere with rehabilitation.[5] It has been claimed that there is an independent association between UTI and poor stroke outcome.[4] Therefore, prevention and prompt treatment of UTI in stroke patients might improve outcome.

We aimed to establish the incidence of UTI, determine the risk factors associated with its development, and explore the impact of UTI on

Address correspondence to Prof. D.J. Stott, Academic Section of Geriatric Medicine, Third Floor, Queen Elizabeth Building, Glasgow Royal Infirmary, Glasgow G31 2ER, UK. email: d.j.stott@clinmed.gla.ac.uk

stroke outcome in a prospective cohort of acute stroke patients.

Methods

A prospective cohort study was carried out of 412 consecutive admissions to a large urban teaching hospital during a 17-month period from June 2004 until November 2005. We have previously published on the incidence of chest infection in this study cohort.[22] The inclusion criterion was first or recurrent ischaemic or haemorrhagic stroke within 7 days of admission. We excluded patients who presented >7 days after admission or who were confirmed to have a non-stroke diagnosis. The diagnosis of stroke was made on clinical grounds supported by computed tomography or magnetic resonance imaging brain scans. Patients or their relatives consented to this study, which was approved by the Multicentre Research Ethics Committee for Scotland.

We recorded pre-morbid functional level as defined using the 20-point Barthel Index[23] and Rankin scale,[24] and severity of stroke was determined using the modified National Institutes of Health Stroke Scale,[25] post-stroke Barthel Index and Rankin scale. Cognitive function was assessed using the 10-point Abbreviated Mental Test (AMT).[26] Patients were followed up for 3 months. Median length of hospital stay was 17 days. We recorded in-hospital clinician diagnosis of UTI, and the date this diagnosis was made. The diagnosis of UTI was made independently of the researcher who gathered the clinical data. We recorded, if the patients had symptoms of dysuria or were catheterized. The results of urine dipstick test for nitrites were recorded. Positive urine culture was accepted if there were white blood cells and $\geqslant 10^5$ bacteria per millimetre of urine. Admission bloods included serum urea and albumin levels. Maximal white blood cell count and C-reactive protein (CRP) were recorded.

The data were analysed using the SPSS software (version 15.0). We compared those patients diagnosed with UTI vs. those who were not. Normally distributed continuous variables are summarized as mean and standard deviation and were compared using unpaired students *t*-test (two-tailed). Non-normally distributed continuous variables were summarized as median and inter-quartile range (IQR) and analysed using the Mann–Whitney U-test. The categorical variables were summarized as number (and percentage) and analysed using the chi-squared test. Binary logistic-regression analysis (forward logistic regression) was performed with the dependent variable diagnosis of UTI and independent variables potential risk factors for development of UTI; these included sex, pre-stroke Rankin, history of stroke, diabetes, AMT score, mNHISS, post-stroke Rankin, serum urea and albumin levels, urinary catheter, pneumonia (Mann criteria)[22] and age by decade. A further logistic-regression analysis was performed with the dependent variable death or disability (modified Rankin Scale > 3) at 3 months after stroke, and independent variables including age, pre-stroke morbidity, severity of stroke and post-stroke infections including urinary tract.

Results

The study recruited 412 stroke patients; 65 (15.8%) were diagnosed as having had UTI during the study, at a median of 14 (IQR = 4–39) days after stroke onset (Figure 1).

On univariate analysis, they were more likely to be older and be more functionally dependent prior to their stroke when compared with those who did not develop a UTI (Table 1). Those who were

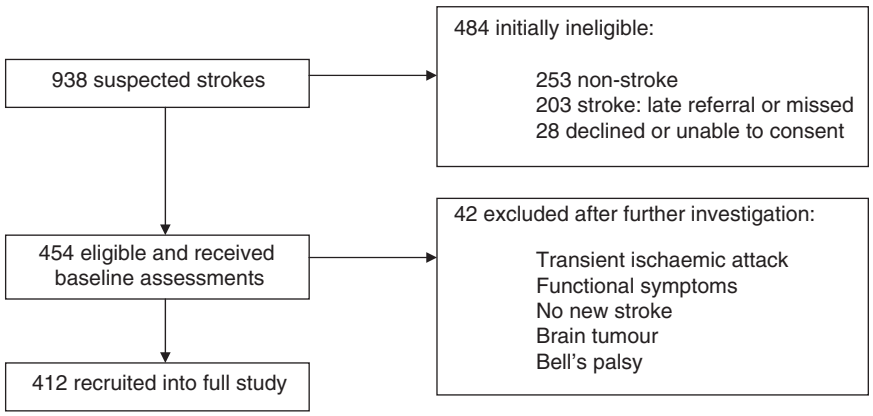

Figure 1. Flow diagram for recruitment of patients to study.

diagnosed with UTI were more likely to have had a more disabling stroke as shown by their mNHISS and post-stroke Rankin scores, and to have a lower AMT score; they were also more likely to have had a urinary catheter or symptoms of dysuria. Positive dipstick test for nitrites or positive urine culture was more common in those diagnosed with UTI compared with those with no UTI. There were also statistically significant differences in the highest recorded white blood cell counts and CRP, which were higher in those diagnosed with UTI when compared with those who had no UTI. The incidence of pneumonia and other bacterial infections was greater in those who developed a UTI. The univariate analysis revealed no statistically significant differences between the two groups when comparing their gender, history of diabetes or maximum temperature on admission (Table 1).

The data were further analysed by binary logistic regression (forwards stepwise) (Table 2). The dependent variable was UTI/no UTI, and the independent variables were gender, pre-stroke Rankin scale, history of diabetes, Abbreviated Mental Test score,[26] mNHISS score,[25] post-stroke Rankin scale, serum urea and albumin, use of urinary catheter, diagnosis of pneumonia and age by decade. This analysis revealed increasing age, greater stroke severity as demonstrated by post-stroke Rankin scale and catheterisation to be independently associated with increased risk of developing UTI.

In univariate analysis, UTI was associated with poor outcome at 3 months including increased risk

Table 1 Clinical characteristics and basic laboratory investigations in stroke patients who developed urinary tract infection compared with those with no UTI

	No UTI	Diagnosis of UTI	*P*-value	Odds ratio (95% CI)
Numbers (%)	347 (85.7%)	65 (15.8%)	–	–
Age, years	66.4 (14.0)	75.7 (10.5)	<0.001	1.79 (1.41–2.28)
Sex (female:male)	169:178	38:27	0.149	1.48 (0.87–2.53)
Pre-stroke morbidity				
Previous stroke	139/347 (40.1%)	29/65 (44.6%)	0.493	1.20 (0.70–2.05)
Diabetes mellitus	57/347 (16.4%)	13/65 (20.0%)	0.481	1.27 (0.65–2.50)
Pre-stroke modified Rankin scale (median and IQR)	0 (0,1)	0 (0,2)	0.003	1.37 (1.09–1.73)
Number of medications	5.6 (4.0)	6.2 (3.8)	0.137	1.04 (0.98–1.12)
Admission clinical and laboratory characteristics				
Cerebral haemorrhage: infarct	18:329	3:62	0.847	1.13 (1.09–1.18)
OCSP: Total anterior circulation stroke	55/347 (15.9%)	25/65 (38.5%)	<0.001	3.32 (1.86–5.91)
mNIHSS score (median and IQR)	4 (2,9)	10 (6.25,17)	<0.001	1.13 (1.09–1.18)
Post-stroke mRS	3 (2,4)	4 (4,5)	<0.001	2.57 (1.92–3.44)
Abbreviated mental test	9 (5,10)	4 (0,7.5)	<0.001	0.84 (0.79–0.90)
Heart rate/min	82.2 (20.8)	89.8 (21.5)	0.008	1.17 (1.04–1.32)
Serum urea (mmol/l)	6.4 (3.1)	7.8 (3.7)	0.003	1.11 (1.03–1.19)
Serum albumin (g/l)	40.4 (5.6)	38.4 (5.9)	0.008	0.94 (0.90–0.98)
Clinical characteristics and laboratory investigations during hospital stay post-stroke				
Dysuria	2/338 (0.6%)	22/65 (33.8%)	<0.001	90.2 (20.5–397.4)
Urinary catheter	63/339 (18.6%)	41/65 (63.1%)	<0.001	7.48 (4.22–13.28)
Urinary nitrites positive (dipstick)	30/339 (8.8%)	48/65 (73.8%)	<0.001	33.0 (16.5–65.7)
Positive urine culture	17/364 (4.9%)	52/65 (80%)	<0.001	77.4 (35.5–168.7)
Pneumonia (Mann Criteria)	52/346 (15.0%)	26/65 (40.0%)	<0.001	3.77 (2.17–6.71)
Other bacterial infections	25/342 (7.3%)	20/65 (30.8%)	<0.001	5.64 (2.90–10.97)
Maximum temperature (°C)	36.9 (1.0)	37.0 (0.9)	0.293	1.18 (0.87–1.61)
Maximal white blood cell count (10^9/l)	11.4 (7.7)	14.7 (5.5)	0.001	1.06 (1.01–1.12)
Maximal CRP, mg/l (median and IQR)	14 (6,48)	117 (36,182)	<0.001	1.009 (1.006–1.012)

OCSP: Oxford Community Stroke Programme; mNIHSS: Modified National Institutes of Health Stroke Scale; Results of categorical data are expressed as numbers (%) or a ratio, continuous data are summarized as mean (SD), except where stated. Statistical analyses are by unpaired student's *t*-tests (normally distributed continuous data), Mann–Whitney U-test (non-normally distributed continuous data) and chi-squared (categorical data), with univariate OR and 95% CIs. All analyses are two-tailed.

Table 2 Predictors of UTI after stroke; multivariate binary logistic regression analysis

		Significance	OR (95% CI)
Step 1	Urinary catheter	<0.001	7.60 (4.01–14.39)
Step 2	Post-stroke mRS	<0.001	2.07 (1.46–2.93)
	Urinary catheter	0.004	3.00 (1.42–6.36)
Step 3	Post-stroke mRS	0.001	1.85 (1.29–2.64)
	Urinary catheter	0.005	3.03 (1.41–6.52)
	Age decade	0.005	1.51 (1.13–2.00)

Binary logistic regression analysis (forward stepwise) was performed with the dependent variable UTI/no UTI. Independent variables were sex, pre-stroke modified Rankin scale, history of stroke, diabetes, Abbreviated Mental Test score, modified National Institutes of Health Stroke Scale score, post-stroke modified Rankin scale, serum urea, albumin, urinary catheter, pneumonia (Mann criteria) and age by decade.

Table 3 Urinary tract infection after stroke and death or disability at 3 months

	No UTI	Diagnosis of UTI	*P*-value	OR (95% CI)
Death	46/345 (13.3%)	21/65 (32.3%)	<0.001	3.10 (1.69–5.68)
mRS (median, IQR)	2 (1–3) $n=296$	3 (2.75–4.25) $n=42$	<0.001	1.79 (1.41–2.28)
Death or disability (mRS > 3)	100/342 (29.2%)	41/63 (65.1%)	<0.001	4.51 (2.56–7.96)

Results of categorical data are expressed as numbers (%), continuous data are summarized as median (IQR). Statistical analyses are by Mann–Whitney U-test (non-normally distributed continuous data) and chi-squared (categorical data), with univariate OR and 95% CIs.

Table 4 Predictors of death or disability (modified Rankin Scale > 3) at 3 months after stroke

	Significance	OR (95% CI)
Age decade	0.284	1.138 (0.899–1.440)
Female gender	0.882	1.048 (0.562–1.954)
Pre-stroke mRS	0.035	1.357 (1.022–1.803)
History of stroke	0.283	1.422 (0.748–2.701)
Number of medications	0.495	1.028 (0.950–1.111)
mNIHSS	<0.001	1.156 (1.073–1.245)
Post-stroke mRS	0.040	1.444 (1.016–2.053)
UTI	0.120	1.903 (0.845–4.284)
Pneumonia (Mann criteria)	0.115	1.951 (0.850–4.476)
Other bacterial infection	0.755	1.171 (0.434–3.163)

mNIHSS: modified National Institutes of Health Stroke Scale
Binary logistic regression analysis was performed with the dependent variable death or disability (mRS > 3) at 3 months after stroke. Independent variables were age, gender, pre-stroke Rankin, history of stroke, number of medications, mNIHSS, post-stroke mRS, UTI, pneumonia (Mann criteria) and other bacterial infections. Multivariate analysis including age, pre-stroke morbidity, severity of stroke and post-stroke infections including urinary tract.

of death (OR = 3.10, 95% CI = 1.69–5.69), higher modified Rankin scale (mRS) (OR = 1.79, 1.41–2.28), and the combined endpoint of death or disability (mRs > 3) (OR = 4.51, 2.56–7.96) (Table 3). However, in multivariate binomial regression analysis that included measures of stroke severity (mNIHSS, mRS) and pre-stroke morbidity (pre-stroke mRS, history of stroke, number of medications), these associations were attenuated and UTI was not a statistically significant

independent predictor of outcome with UTI showing a multivariate OR of 1.903 (95% CI = 0.845–4.284) for the combined endpoint of death or disability (Table 4).

Discussion

We found an in-hospital incidence of UTI of 15.8% in our patients following an acute stroke. These data are generally in keeping with several other studies of acute stroke subjects with reasonable length of follow-up. In Indredavik's series of 489 unselected acute stroke admissions, there was an UTI incidence of 16% in the first week and 27.9% at 3 months.[18] Davenport found an in-hospital UTI incidence of 16% in 613 consecutive acute stroke admissions.[1] We have previously published on a multicentre study of 311 consecutive acute stroke admissions where the in-hospital incidence of UTI was 24%.[6] A large study (1455 patients) of acute ischaemic stroke patients recruited to a randomized controlled trial found an incidence of 17.2% of UTI.[4] However, there is wide variation reported in the later incidence of UTI, of between 14% and 44% of stroke patients in a specialist stroke rehabilitation facility.[3,9,11,14,19–21] This may reflect differences in selection of patients and in case mix. Studies of acute stroke that have reported a very low UTI incidence of 3–4% have had very short follow-up, as brief as 48 h.[16,17]

It has been claimed that UTI is a risk factor for the development of stroke,[7] possibly causing systemic inflammation and activation of thrombosis. Therefore, it might be expected that some UTIs would be identified in acute stroke patients on admission. However, it appears from our data and other studies[1,15,17] that diagnosis of UTI within 48 h of admission is relatively unusual, and most UTIs develop after hospital admission as a nosocomial infection. The median time to developing UTI in our study population was 17 days, similar to that observed by Davenport *et al.*[1] of around 15 days.

Our study identified increasing age, urinary catheterization and stroke severity as independent predictors of incident UTI after stroke. Other studies of acute stroke have also found age[4] and stroke severity[4,18] to be independent risk factors. We did not find an independent association of UTI with diabetes mellitus, as has been claimed in one study[13] or with female gender as reported by Aslanyan *et al.*[4] We found a strong association of urinary catheterization with UTI. Urinary catheterization has been reported in univariate analysis to be associated with post-stroke UTI in a study of a rehabilitation unit cohort.[3] This association is as expected from studies of more general non-stroke hospital populations,[27,28] in whom there is an incidence of around 5% per day of catheter-associated UTI.[27]

We found a strong association of dysuria with diagnosis of UTI. Dysuria is associated with UTI in young women, with an OR of 1.5[29] but its diagnostic utility has not been reported post-stroke. Our data suggest that when dysuria is recorded after stroke, it is highly likely that the patient has a UTI. However, many stroke patients with UTI do not have dysuria. This lack of sensitivity may be at least partly due to post-stroke communication barriers to reporting of symptoms such as dyphasia, confusion or depressed conscious level.

There are biologically plausible reasons for UTI causing a worse outcome after stroke. In the acute phase, UTI-induced systemic inflammation and raised temperature[30] may increase the damage to vulnerable brain tissue in the ischaemic penumbra.[31,32] Infections also are associated with a catabolic response, with loss of skeletal muscle; this likely to be due to multiple complex factors, including inflammation and cytokine release, increased glucocorticoids and activation of the sympatho-adrenal axis.[33] The associated loss of skeletal muscle is likely to adversely affect physical rehabilitation. We found that UTI was associated with increased risk of death and/or post-stroke disability at 3 months after stroke. However, these associations were attenuated and became non-significant when other factors, including measures of severity of stroke and pre-stroke disability, were included in a multivariate analysis. However, our data lack statistical power for stroke outcome, and we cannot exclude a clinically relevant independent contribution of UTI to poor stroke outcome. There are limited published data on the association of post-stroke UTI with outcome; however one study found UTI was independently associated with long-term disability.[4]

Our study does have a number of limitations. We accepted a diagnosis of UTI by the attending physician, and did not employ strict pre-defined criteria. As a result we may have over-diagnosed UTI, as some patients may have been inappropriately diagnosed and treated for asymptomatic bacteriuria. However, the patients diagnosed as UTI did as a group have evidence of clinically significant infection with elevated white blood cell count and CRP, which would suggest the clinician diagnosis was generally valid. We did not gather information on post-void residual urine volume, claimed to be associated with UTI in un-catheterized patients in a rehabilitation cohort, and so we cannot comment on this possible risk factor.[20]

There are a number of possible strategies to prevent UTI post-stroke that are worthy of future study. Avoidance of unnecessary catheterization is likely to be the single most effective strategy in preventing UTI.[34] If a urinary catheter is used it may be possible to reduce the risk of associated infection by early removal, attention to detail in catheter-care or by use of modified catheters coated with antimicrobials. A programmed reminder to nurses by physicians to remove unnecessary catheters in ITU has been shown to reduce duration of catheterization and associated infections.[35] Use of modified catheters such as nitrofurazone-coated silicone or silver-coated latex may reduce the risk of infection with short-term catheterization.[27,36] High standards of catheter care including insertion in an aseptic fashion, correct positioning of the drainage tubing and collection bag and maintaining a closed system may all help to reduce the risks of clinically significant infection.[27] There is evidence that in-hospital care pathways might reduce the incidence of UTI, however, the components of care that achieve this effect are not clear.[37] Further research is also warranted on the potential longer-term benefits of prevention of UTI on stroke outcome, including urinary continence and disability.

Conclusions

UTI is common after acute stroke. The presence of dysuria is highly specific for UTI, but lacks sensitivity. UTI is associated with urinary catheterization, severity of stroke and increasing age. Avoidance of catheterization might reduce the incidence of this common complication.

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