HHS Public Access

Author manuscript

*Urology*. Author manuscript; available in PMC 2021 October 20.

Published in final edited form as:

*Urology*. 2019 January ; 123: 24–27. doi:10.1016/j.urology.2018.09.025.

# Recurrent Urinary Tract Infections are associated with Frailty in Older Adults

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## Abstract

**Objective:** To understand the relationship between frailty, age and recurrent urinary tract infections (rUTIs).

**Materials and Methods:** The Timed Up and Go Test (TUGT), a measure of frailty, was administered to all adults ages ≥65 presenting to an academic non-oncologic urology practice from December 2015 to January 2018. TUGT was categorized as fast (≤10 seconds), intermediate (11–14 seconds) or slow (≥15 seconds). The TUGT and other clinical data were abstracted from the medical record using direct queries supplemented with chart review. Logistic regression was used to determine the relationship between frailty, age and the diagnosis of rUTIs in our clinic population.

**Results:** There were 136 older adults with and 2824 older adults without a diagnosis of rUTIs. Individuals with rUTIs had slower TUGT times (13.8 ± 10.4 seconds compared to 10.8 ± 4.52 seconds, $p<0.01$) and were more likely to be classified as slow, or "frail" (27.2% versus 10.8%). In multivariate analysis, slow TUGT times were associated with a diagnosis of rUTIs (adjusted OR 2.0, 95% CI 1.2–3.3), while age was not a statistically significant predictor of this diagnosis (adjusted OR 1.3, 95% CI 0.7–2.2 for ages ≥81 years).

**Conclusions:** Older adults with a diagnosis of rUTIs are significantly more frail compared to those with other non-oncologic urologic diagnoses. Frailty (adjusted for age), was significantly associated with rUTIs, while age (adjusted for frailty) was not. Furthermore, frailty (rather than age) may be important to consider when caring for and treating older adults with rUTIs.

### Keywords

TUGT (timed up and go test); elderly; urology

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## Introduction

Urinary tract infections (UTIs) are the most commonly diagnosed infection in institutionalized older adults and the second most commonly diagnosed infection among community dwelling older adults. UTIs account for 7–8 million clinic visits, over 100,000 hospital admissions,[1] and cost over $2.6 billion per year in the United States alone.[2] Some older individuals experience recurrent UTIs (rUTIs), which are defined as three or more infections in a period of 12 months or 2 or more infections in a period of 6 months.[3]

The literature suggests that the incidence and prevalence of rUTIs increase with age. This age-related increase has been attributed to several potential precipitating factors such as the presence of chronic diseases, certain medications, lack of estrogen, urinary and fecal incontinence, pelvic organ prolapse, increased post void residual volumes, and poor hygiene.[4,5] However, frailty, which represents a multifactorial syndrome manifested by a reduction in physiologic reserve and an increased susceptibility to stressors,[6] is also associated with increasing age and may have an even more significant association with rUTIs than age alone. Our prior work demonstrated that older adults with diagnoses of UTIs were, on average, more frail compared to older adults with other non-oncologic urologic conditions presenting to our academic clinical practice.[7] The relationship between frailty, age and rUTIs, however, remains unknown.

In order to examine these relationships further, we used data from the University of California, San Francisco Geriatric Urology Database (UCSF-GUD). This is a prospectively collected database that includes the Timed Up and Go Test (TUGT) as a measure of frailty for all outpatient visits in our non-oncologic urology clinical practice. Findings from this study will help to better understand the relationship between age, frailty and rUTIs in older adults and potentially lay the groundwork for a new conceptual model for understanding rUTIs in this population.

## Materials and Methods

### Patients and Database

We used data from the UCSF-GUD from December 1, 2015 to January 31, 2018. This is an institutional review board (IRB) approved database that prospectively collects data on all individuals ages 65 and older presenting to the UCSF non-oncologic urology clinical practice for either a new or follow up patient visit. Data are entered into the electronic medical record (EPIC) in real time and are regularly extracted from EPIC using extract, transform and load routines via the clinical data reporting database (Clarity) and data mart (Cogito). Details on this process have been previously published.[7,8]

There were a total of 4088 unique individuals in the database during the study period. Out of these individuals, 2960 (72.4%) had a TUGT value and were included in the study cohort. Individuals with a UTI diagnosis were identified using International Statistical Classification of Diseases (ICD-9 and ICD-10) codes listed in the Supplemental Table. There were 363 individuals with at least one code of interest and a TUGT value documented within 180 days of the date that the code appeared in the medical record.

Next, we performed a thorough retrospective chart review of each of these 363 individuals with the codes of interest. Individuals were included in the rUTI arm of the study if they had at least 2 culture-proven UTIs during a 6-month period or 3 culture-proven UTIs during a 12-month period. UTIs had to be at least 14 days apart to be considered separate infections. Exclusionary criteria included cultures that grew Group B Strep or mixed flora, individuals who were documented as being asymptomatic in the setting of a positive culture, individuals who had any genitourinary surgery in the 3 months prior to the date of the urine culture or those with any urinary tract reconstruction (such as an ileal conduit or neobladder).

### Covariates

The TUGT was used as our measure of frailty. This test was performed on all patients ages 65 and older presenting to our non-oncologic urology clinical practice and was administered alongside the vitals. As part of this test, patients were instructed to stand up from a chair, walk 10 feet to a mark on the floor, turn around and sit back down in the chair. Completion of this test includes assimilation of cognition (understanding and following instructions), speed, balance, and core strength (required to stand up and sit down into a chair). The TUGT can be categorize as “fast” (≤10 seconds), “intermediate” (11–14 seconds), and “slow” (≥15 seconds). Slower TUGT times have been shown to be associated with frailty, and hence, with corresponding morbidity and mortality.[9,10] Individuals who are non-ambulatory (i.e. in a wheelchair or gurney) were unable to perform the TUGT and were excluded from the analyses. The TUGT time that most closely correlated with the date of the first documented UTI was used for individuals with more than one office visit during the study period. Additional covariates included gender, age (65–70, 71–75, 76–80, ≥80 years), race (white and non-white), and number of medications (0–5, 6–8, 9–12, 13–44) and body mass index (BMI).

### Statistical Analysis

Summary characteristics were compared between individuals with and without a diagnosis of rUTI and were presented as averages with standard deviations or as numbers with percentages, where appropriate. Groups were compared using Mann-Whitney and Chi-square t tests, where appropriate, with 2-sided P values of $<0.05$. Multivariable logistic regression was performed with the diagnosis of rUTI as the dependent variable. Covariates included gender, age, race, number of medications, BMI and TUGT. A second model was created to explore an interaction term between age and TUGT. Analyses were preformed using SAS 9.3 software.

## Results

There were a total of 2,960 unique patients with a TUGT in our database from December 1, 2015 to January 31, 2018, 136 of which had a verified diagnosis of rUTIs based on extensive chart review (Table 1). Overall, the cohort was predominantly male (75.4%), however, patients with rUTIs were more likely to be female (69.1% versus 22.4%; $p<0.01$). Additionally, individuals with rUTIs were on more medications (average 11.6 ± 5.9 versus 9.0 ± 5.3 medications; $p<0.01$) and had slower TUGT times (average 13.8 ± 10.4 seconds versus 10.8 ± 4.5 seconds; $p<0.01$) and 27.2% versus 10.8% had TUGT ≥15 seconds

(p<0.01) compared to the non-rUTI individuals in the cohort. Of note, age, race and BMI were not statistically significantly different between the two groups.

Results of the logistic regression predicting a diagnosis of rUTI (as opposed to another non-oncologic urologic diagnose) are presented in Table 2. A TUGT ≥15 seconds was associated with increased odds of a diagnosis of rUTI (adjusted OR 12.0; 95% CI 1.2–3.3; p=0.01). Other statistically significant associations with a diagnosis of rUTI included female gender (adjusted OR 7.5; 95% CI 5.0–11.1; p<0.01) and 13–44 medications (adjusted OR 2.2; 95% CI 1.3–3.9; p<0.01). Non-white race was associated with lower odds of a diagnosis of rUTIs (adjusted OR 0.7; 95% CI 0.5–1.0; p<0.01). Of note, age was not statistically significantly associated with a diagnosis of rUTIs (adjusted for age ≥81 years 1.3; 95% CI 0.7–2.2; p=0.39). An interaction term between age and TUGT was added to a separate model and was not found to be statistically significant (not shown).

## Discussion

Patients with a diagnosis of rUTIs have significantly slower TUGT times, which is associated with frailty, compared to patients seeking care for other non-oncologic urologic diagnoses in our clinical population. The association between TUGT and a diagnosis of rUTIs remains significant even after adjusting for other factors including age, gender, race, number of medications, and BMI. Interestingly, age (adjusted for TUGT, gender, race, number of medications, and BMI) is not statistically significantly associated with a diagnosis of rUTI.

This is the first study to investigate the association of frailty with rUTIs among older adults. We found that 27.2% of patients with rUTIs were frail, compared to only 10.8% of patients with other non-oncologic urologic diagnoses, representing an almost 3-fold higher prevalence of frailty among this population. The average TUGT score among our rUTI population was 13.8 seconds compared to 10.8 seconds among patients with other non-oncologic urologic diagnoses. These findings are similar to what we previously found in older adults with a diagnosis of overactive bladder (OAB), where the mean TUGT time was 13.7 seconds.[8] To put these findings into context, the literature reports average TUGT times for community-dwelling older adults to be 8 seconds for men and women ages 60–69, 9 seconds for men and women ages 70–79 and 10 seconds for men and 11 seconds for women ages 80–89.[11] Furthermore, patients presenting to our practice were more frail overall (with patients with a diagnosis of rUTI being much more frail) compared to community-dwelling age-matched individuals.

Our finding that TUGT (adjusted for age) is significantly associated with a diagnosis of rUTI, while age (adjusted for TUGT) is not, suggests that frailty may have a more important association with rUTIs than previously realized. This concept challenges our current understanding of rUTIs as primarily an age-related condition and introduces the notion that it may instead be more of a frailty-related phenomenon. Frailty, which is a multifactorial syndrome manifested by a reduction in physiological reserve and in the ability to resist stressors,[6] is a much more dynamic process than aging alone.

This study should be considered with certain limitations in mind. First, the UCSF-GUD represents data from only one academic non-oncologic urology setting and findings may represent patients who are more complex, sick, or frail, compared to other clinical populations. Despite this potential limitation, we believe that our practice is likely similar to other academic practices and serves as a good starting point for measuring and understanding these associations. Future studies in different types of clinical settings are needed to address the potential generalizability of our findings. Second, we used the TUGT as our measure of frailty, which is one of many potential measures of this construct. The TUGT has a sensitivity of 0.93 and a specificity of 0.62 for frailty, indicating that there may be a high false positive rate of frailty in our study based on the definition.[12] While we recognize that there is no one perfect measure of frailty, we chose the TUGT since it is parsimonious, simple and quick to administer in the busy clinical setting and has established documented associations with complications and increased 1-year mortality among surgical populations.[9]

## Conclusions

Frailty, as measured by the TUGT, is significantly associated with a diagnosis of rUTIs in our clinical population. This finding persists, even after adjustment for other important factors including age. Contextualization of rUTIs in the setting of frailty represents a paradigm shift in how we understand and treat older adults with this condition, highlighting the need for additional care and thoughtfulness when selecting management strategies for this condition among this particularly vulnerable population. Further investigation is warranted to better explore and understand this finding, the possible mechanisms underlying the association between frailty and rUTIs, and implications of various treatments for this condition among this unique population.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

Funding: National Institute of Diabetes and Digestive and Kidney Diseases University of California, San Francisco KURe Career Development Program (K12 DK83021-07); Medical Student Training in Aging Research Program, the National Institute on Aging T35AG026736; UCSF CTSI Scholars Program; UCSF Claude D. Pepper Older Americans Independence Center

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**Table 1.**

Demographic characteristics of cohort

| Variable | Total | UTI (N=136) | Non-UTI (N=2824) | P-Value |
|---|---|---|---|---|
| Age (Mean ± SD) | | 74.3 ± 6.9 | 73.3 ± 6.5 | 0.13 |
| Age | | | | |
| 65–70 | 1201 (40.6%) | 51 (37.5%) | 1150 (40.7%) | 0.24 |
| 71–75 | 800 (27.0%) | 32 (23.5%) | 768 (27.2%) | |
| 76–80 | 519 (17.5%) | 25 (18.4%) | 494 (17.5%) | |
| 81+ | 440 (14.9%) | 28 (20.6%) | 412 (14.6%) | |
| Gender | | | | |
| Male | 2233 (75.4%) | 42 (30.9%) | 2191 (77.6%) | <0.01 |
| Female | 727 (24.6%) | 94 (69.1%) | 633 (22.4%) | |
| Race | | | | |
| White | 1926 (65.1%) | 95 (69.9%) | 1831 (64.8%) | 0.40 |
| Non-White | 946 (32.0%) | 40 (29.4%) | 906 (32.1%) | |
| meds (Mean ± SD) | | 11.6 ± 5.9 | 9.03 ± 5.3 | <0.01 |
| Number of Medications | | | | |
| 0–5 | 768 (25.9%) | 22 (16.2%) | 746 (26.4%) | <0.01 |
| 6–8 | 723 (24.4%) | 19 (14.0%) | 704 (24.9%) | |
| 9–12 | 781 (26.4%) | 38 (27.9%) | 743 (26.3%) | |
| 13–44 | 688 (23.2%) | 57 (41.9%) | 631 (22.3%) | |
| BMI (Mean ± SD) | | 27.2 ± 4.9 | 26.9 ± 4.9 | 0.59 |
| TUGT (Mean ± SD) | | 13.8 ± 10.4 | 10.8 ± 4.5 | <0.01 |
| TUGT | | | | |
| Fast (<= 10 sec) | 1760 (59.5%) | 59 (43.4%) | 1701 (60.2%) | <0.01 |
| Intermediate (11 to 14 sec) | 858 (29.0%) | 40 (29.4%) | 818 (29.0%) | |
| Slow (>= 15 sec) | 342 (11.6%) | 37 (27.2%) | 305 (10.8%) | |

**Table 2.**

Model predicting a diagnosis of rUTIs among patients presenting to an academic non-oncologic urologic practice

| Value | Outcome/Total (%) | Odds Ratio | Lower 95% CI | Upper 95% CI | P-Value |
|---|---|---|---|---|---|
| Age | | | | | |
| 65–70 | 50/1161 (4.3%) | 1.0 | | | |
| 71–75 | 32/778 (4.1%) | 0.9 | 0.5 | 1.4 | 0.54 |
| 76–80 | 25/505 (5.0%) | 1.0 | 0.6 | 1.6 | 0.87 |
| 81+ | 28/428 (6.5%) | 1.3 | 0.7 | 2.2 | 0.39 |
| Gender | | | | | |
| Male | 41/2167 (1.9%) | 1.0 | | | |
| Female | 94/705 (13.3%) | 7.5 | 5.0 | 11.1 | <0.01 |
| Race | | | | | |
| White | 95/1926 (4.9%) | 1.0 | | | |
| Non-White | 40/946 (4.2%) | 0.7 | 0.5 | 1.0 | 0.07 |
| Number of Medications | | | | | |
| 0–5 | 21/715 (2.9%) | 1.0 | | | |
| 6–8 | 19/707 (2.7%) | 0.9 | 0.5 | 1.7 | 0.69 |
| 9–12 | 38/770 (4.9%) | 1.4 | 0.8 | 2.6 | 0.21 |
| 13–44 | 57/680 (8.4%) | 2.2 | 1.3 | 3.9 | <0.01 |
| BMI (per 5-unit increase) | 129/2639 (4.9) | 1.0 | 0.8 | 1.2 | 0.89 |
| TUGT | | | | | |
| Fast (<= 10 sec) | 58/1700 (3.4%) | 1.0 | | | |
| Intermediate (11 to 14 sec) | 40/839 (4.8%) | 1.2 | 0.8 | 1.9 | 0.40 |
| Slow (>= 15 sec) | 37/333 (11.1%) | 2.0 | 1.2 | 3.3 | 0.01 |