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Mini Review

Frailty associated urinary tract infections (FaUTIs)

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Abstract

This review summarizes the current literature on the correlation between frailty and urinary tract infections (UTIs), as well as the potential causes and measures that can be taken to prevent and treat these frailty associated UTIs (FaUTIs). A narrative review of the literature was carried out using the keywords and other associated terms (catheter associated UTIs and frailty, causes of UTIs, prevention of UTIs in the frail, treatment of UTIs in the frail). As it is shown in the literature, many risk factors that are associated with frailty such as dehydration, reduced mobility and cognitive impairment, as well as other anatomical or functional abnormalities can make frail patients prone to UTIs that are also more difficult to treat. Early correction of these risk factors (for example avoiding long term catheters, increasing hydration, treating lower urinary tract obstruction or incontinence), can prevent UTIs and improve the quality of life of frail patients. Prompt and individualized antimicrobial treatment of UTIs in the frail population can result in decreasing mortality rates but also minimize unnecessary antimicrobial drug use.

Keywords: Frailty, Infections in the frail, Prevention of UTIs, Urinary tract infections, Urosepsis

Introduction

Frailty syndrome is an age-related clinical condition in which someone is prone to negative health associated outcomes such as reduction in physical activity, disability and hospitalizations[1]. In particular, frail individuals are vulnerable to all these outcomes when exposed to stressors, both endogenous and exogenous[1]. These stressors may have different consequences concerning people with frailty to achieve complete recovery of their former health status[1]. Nowadays, health care professionals have to deal with increasingly older patients and their decline in functioning among multiple systems of their body[2]. Therefore, over the past 20 years, assessment tools and indexes have been developed in order to identify people who are at great risk for adverse health associated outcomes related to frailty[3,4]. Moreover, these tools and indexes may allow us to detect frail individuals perioperatively and determine our treatment strategy for frail surgical patients in order to reduce postoperative complications[4,5].

Urinary tract infections (UTIs) are infectious diseases which are very common in humans and are caused by bacteria entering urethra, developing in the bladder and spreading to kidneys. They can be located in any part of the urinary tract[6]. Apart from uncomplicated UTIs which can resolve either spontaneously or with antibiotics, there are also more complicated forms such us catheter-associated UTI (CaUTI), recurrent UTI (rUTI), male UTIs[7]. The accurate diagnosis of these infections and early treatment play a pivotal role due to risk of recurrence, septicaemia and long-term consequences[8]. UTIs are a considerable cause of morbidity among elders[9]. However, the global antibiotic use for UTIs and their recurrence has led to increased antibiotic resistance making their treatment particularly challenging[10].

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This paper reviews the interplay between frailty syndrome and urinary tract infections and their potential recurrence.

Association between frailty and urinary tract infections

Important tools to evaluate the degree and severity of frailty are the various frailty indexes, calculators and scores. These indexes have been used to measure the vulnerability of patients to several diseases and to predict complications after conservative and surgical treatment of these diseases[4]. The use of frailty indexes has been shown to be crucial in assisting physicians to choose the most suitable treatment for their patients and to avoid unnecessary complications. Furthermore, it has been shown that altering and improving some of these factors of frailty, such as muscle loss with preoperative exercise, management of iron deficiency and anemia, malnutrition and sarcopenia, can lead to better outcomes from the treatment of these patients[4,11-13].

A prospective study by Tang et al. (2019) collected data from an institutional review board approved database that includes the Timed Up and Go Test (TUGT) as a measure of frailty for all outpatient visits in their nononcologic urology clinical practice. The aim of the study was to investigate whether there is any association between frailty and recurrent Urinary Tract Infections (UTIs). They concluded that recurrent UTIs are significantly more frequent in frail patients irrespective of their age. Thus, frailty has to be considered as a more important factor in the treatment and follow up of patients with recurrent UTIs than advanced age[14].

The risk of UTIs and sepsis has also been shown to be higher in patients with more advanced frailty status after urological interventions and major or minor urological or other surgical procedures[15-17]. Amin et al. (2019) using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database, showed that during the first 30 postoperative days, complications including UTIs are much more frequent amongst patients with higher ASA (American Society of Anesthesiologists) score, NSQIP frailty index, simplified frailty index, and Risk Analysis Index with the ASA score being the most accurate predictor of complications[15].

Apart from that, Boysen et al. (2017), showed that a combination of procedures in frail patients can lead to more UTIs. More specifically, frail women that underwent an incontinence procedure simultaneously with minimally invasive sacrocolpopexy had an increased postoperative risk for urinary tract infections, but not for other early postoperative complications[18].

Association between frailty and urosepsis

In a population-based cohort in primary care published earlier this year by Gulliford et al it was shown that there is an increased risk for development of sepsis in frail patients that have an episode of acute urinary infection. The risk of sepsis was found to be higher in urinary infection in comparison to skin and respiratory infections irrespective of the age of the patients. In addition to this, the administration of antibiotics significantly reduced the risk of sepsis especially in the elderly and more frail patients while their use can be reduced safely in the younger populations[19].

Association between frailty and catheter associated UTIs

Urinary tract infections are often associated with foreign objects such as urinary catheters. An UTI that occurs in a person who has an indwelling catheter or has been catheterised within the past 2 days is considered a catheter-associated UTI (CaUTI) and should be treated as a complicated UTI[20]. The use of catheters is much more common in elderly and frail patients who are also known to be more prone to UTIs. The prevention of CaUTIs includes avoiding the use of catheters wherever possible, limiting the duration of indwelling catheters and choosing alternative methods in cases that necessitate the artificial emptying of the bladder or the monitoring of urine output. Examples of alternative methods include the use of condom catheters for monitoring the urine output and in cases of incontinence, or the teaching of intermittent self-catheterization in patients with detrusor underactivity or bladder outflow obstruction[21,22].

Furthermore, long term suprapubic catheters have been linked with less CaUTIs than permanent indwelling urethral catheters in patients living in nursing homes[23]. Patients with urethral catheters have double the risk of hospitalization and are 23% more likely to need antibiotic treatment. However, patients with suprapubic catheters tend to be more prone to being colonized by multidrug- resistant organisms[23].

Apart from the above, it is of utmost importance that nursing and medical staff irrespective of the specialty should be well trained on the insertion of urinary catheters, so that urethral injuries that can potentially lead to infections can be prevented[21]. The perioperative care of the elderly and frail patients and their catheters is crucial and can also prevent the high risk of UTIs in these populations[21]. It is important to remove the urethral catheter as soon as possible in patients that have undergone an operation or after a serious infection or injury[21].

According to the European Association of Urology guidelines on CaUTIs, the most important risk factor for CaUTIs is the duration of catheterization. Indwelling catheters provide the necessary surface for bacterial colonization and increase the residual urine in the bladder underneath the balloon of the catheter[20]. The main recommendations of the EAU guidelines concerning the treatment of CaUTIs, emphasize on the importance of limiting the duration of indwelling catheters and of proving the presence of infection before actively treating, with a urine culture after placing a new catheter or from mid-stream urine after removing the old. It is also stated that

pyuria or cloudy and odorous urine should not be treated with prophylactic antibiotics in asymptomatic patients, or during the removal or change of a catheter[20].

In a multicentre, multinational retrospective cohort study it was shown that CaUTIs are the most usual cause of complicated UTIs in hospitalized adults who were more likely to be older and more frail patients with higher Charlson comorbidity index. Furthermore, patients with CaUTIs had much higher risk of death than patients with other types of complicated UTIs, although a direct connection between these mortality rates and the CaUTIs could not be established[24].

Asymptomatic bacteriuria and frailty

Asymptomatic bacteriuria is common among frail patients and elderly individuals in care homes. According to the European Association of Urology most recent guidelines this percentage can reach as high as 50%, and is associated with unnecessary antibiotic treatment mainly because of the difficulty in history taking and examination as a result of the impaired cognitive status of these patients. Asymptomatic bacteriuria, should not be treated with antibiotics in elderly or institutionalized patients unless there is evidence of symptomatic UTI or acute infection[20,25].

Asymptomatic candiduria is also very common among very old individuals especially in care homes. The most frequently isolated strain is Candida albicans[26]. In most cases the underlying causes are indwelling urinary catheters and previous antibiotic treatment. Asymptomatic candiduria should not be treated, but if it is associated with an underlying condition, this should be corrected, for example change or removal of indwelling catheters[20,26].

Nevertheless, frail patients with asymptomatic bacteriuria, that undergo urological procedures that breach the urothelial mucosa, such as transurethral resection of prostatic adenoma (TURP), transurethral resection of bladder tumour (TURBT), or ureteroscopy for stone fragmentation (URS), should be treated with a single dose of antibiotics before the procedure, because they have an increased risk for postoperative acute infection and urosepsis. These recommendations are supported by strong evidence from several prospective non-randomized and randomized controlled trials (RCTs)[20,25].

Causes of UTIs and frailty

Frail and older individuals as well as residents at care homes are more prone to UTIs than the rest of the population. Most important reasons for this susceptibility are reduced physical mobility and decreased cognitive status of these patients. As a result of the above, there is a higher possibility of lower fluid intake and dehydration[27,28].

Moreover, a lot of these patients have other coexisting anatomical and functional abnormalities that can also increase the risk of UTIs. More specifically, bladder outflow obstruction caused by benign or malignant prostatic obstruction, resulting in high post-void residual urine in the bladder, which in turn can create the suitable environment for bacterial growth[27]. Long-term urethral catheters can also become colonized by bacteria and cause complicated infections[20,23,27].

Post-menopausal women often suffer from atrophic vaginitis, pelvic organ prolapse and incontinence, all of which are considered risk factors for UTIs[25,27].

Prevention of UTIs and frailty

Preventing UTIs in the frail and elderly individuals is of utmost importance. On the one hand, it can reduce the use of antibiotics and subsequently of their adverse events, and also of the economic burden for the healthcare system[29,30]. On the other hand, the prevention of UTIs can greatly improve the quality of life of these patients, since infections have been associated with more falls and worsening cognitive impairment[25,27].

Increasing the daily fluid intake and ensuring adequate hydration has shown promising results among institutionalized frail patients. Specifically, there are indications that it can reduce the number of UTIs experienced and the number of falls in frail older care home residents[27,28].

The use of continuous low-dose prophylactic antimicrobial treatment for 3-6 months has been found to reduce the episodes of recurrent acute urinary infection in older women in the community. Firstline regimens are nitrofurantoin 50 or 100 mg daily, Fosfomycin trometamol 3 g every ten days, trimethoprim 100 mg once daily and cephalexin 125 mg or 250 mg or cefaclor 250 mg once daily[20,25].

Administration of topical vaginal estrogen has also been proven to decrease the frequency of UTIs in post-menopausal women with atrophic vaginitis. However, the systematic use of estrogen replacement did not show any benefit[20,25].

There is insufficient evidence to suggest that an oral vaccine (OM-89) which is an Escherichia Coli extract can also prevent recurrent UTIs in women. However, the quality of evidence is low with small poorly-reported trials, high heterogeneity and the follow up period for patients receiving the vaccine is limited to 6 months in most of the studies[20,31].

The treatment of any anatomical or functional abnormalities that could be associated to UTIs in the frail is also a successful preventive measure if the patients are fit enough to undergo a corrective procedure. For example, a transurethral resection of the prostatic adenoma in males and correction of pelvic organ prolapse in women can prevent recurrent infections in these patients caused from increased post-void residual urine or incontinence[14].

Treatment of UTIs and frailty

The type and duration of the antimicrobial treatment in older and frail populations may differ depending on the patients' renal function, severity of infection, need for intravenous antibiotics and the cost. A short course regimen with 3 days of an antibiotic such as Cephaclor

or trimethoprim/sulfamethoxazole (TMP/SMX), 5 days of Nitrofurantoin or a single dose of Fosfomycin can successfully treat an episode of acute cystitis in older women in the community, with much fewer side effects and less cost than longer antimicrobial regimens[20,25]. These guidelines concerning antimicrobial courses have a strong grade of recommendation and are based on the susceptibility of the most common pathogens in community, as well as their efficacy in comparative clinical trials, their toxicity and their cost[20,25].

Patients that cannot tolerate oral antibiotics or are septic should receive intravenous antimicrobial treatment depending on previous urine or blood culture sensitivities for 48-72 hours. Antibiotics should be changed to oral as soon as the patient is able to eat and drink and depending on the response to the initial treatment and the results of the more recent blood and urine cultures[20,25].

Complicated UTIs (CaUTIs, acute prostatitis, anatomical abnormalities, pyelonephritis caused by anatomical or functional abnormalities) usually require longer antibiotic regimens between 7-14 days depending on the type of pathogen and the severity of the infection.

If the use of an Aminoglycoside such as Gentamicin or Amikacin is indicated, it is essential to monitor the levels of the drug and the renal function[20,25].

Conclusion

It is widely shown in the literature that frailty is strongly associated to UTIs. Anatomical and functional abnormalities as well as physical and mental impairment of frail patients are the main causes for the increased frequency of infections in these populations. Apart from the increased risk of infections frail patients are also prone to manifest more severe symptoms and sepsis. Prevention of UTIs is of utmost importance in these patients and includes the correction of predisposing factors and changes in their everyday habits. Prompt diagnosis and treatment of UTIs can improve the quality of life of frail individuals, however antimicrobial regimens must be as short as possible to avoid unnecessary drug toxicity and asymptomatic bacteriuria should not be treated.

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