Commentary

To What Extent Does Frailty Influence the Risk of Developing Urolithiasis?

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Abstract: Urolithiasis has become more prevalent in recent years, given the rapid rise of the global geriatric population. Although factors such as ethnicity, dietary and fluid intake, co-morbidity status and age have been associated with increased incidence of urolithiasis, the links between frailty status and risks of developing urolithiasis are not yet known. In this commentary, we will explore the scale and significance of this relationship based on emerging evidence. We will review the plausible factors on how a more severe frailty status may be significantly associated with greater risks of developing urolithiasis. We will also discuss the strategies that may help to lower the incidence of urolithiasis in older and frail individuals. We hope our article will bring greater awareness on this issue and motivate further research initiatives evaluating the relationship between frailty and urolithiasis, as well as holistic prevention strategies to lower the risks of developing urolithiasis within this vulnerable population.

Keywords: frailty; urolithiasis; aging; risk factors; primary prevention

Urolithiasis is a common urological disorder observed in clinical practice and one which may develop into severe complications such as renal tract obstruction, urinary sepsis and kidney injury. Epidemiological evidence on the lifetime prevalence and incidence of urolithiasis appears to be geographically varied, though this is known to be significantly associated with ethnicity, lifestyle issues (such as dietary and fluid intake patterns), co-morbidity status and age [1–4]. Current reports point towards a rising incidence of urolithiasis, most likely explained by the growth of the global geriatric population. Findings from the United States 2007–2010 National Health and Nutrition Examination Survey (NHANES) data note approximately 10.6% and 7.1% of male and female patients in the United States as having urolithiasis during this period [5]. This was a significant increase compared to figures obtained from previous NHANES data over the past few decades prior to the 2007–2010 NHANES. In the NHANES II and III conducted in 1976–1980 and 1988–1994, the prevalence of urolithiasis was 3.8% and 5.2%, respectively [6]. Another national-level population cohort study conducted in South Korea evaluated urolithiasis cumulative incidence differences within an eleven-year period and noted a rise of 5.6 cases per 1000 patient-year between a decade [7]. National registry data in Europe have noted increased incidence of urolithiasis over time as well. The incidence of urolithiasis in Germany has risen by more than 4% between 1979 and 2001 for adults aged ≥ 65, whilst a similar level of increase in incidence of urolithiasis was observed amongst individuals aged 60+ between 1986 and 1998 in an epidemiological study conducted in Milan, Italy [8,9]. The trends in worldwide data suggest more attention should be provided to this emerging health issue.

Due to proposed links between the rising incidence of urolithiasis and our aging population, the presence of any significant associations between frailty status and risks of
developing urolithiasis should be considered. Frailty is an age-associated clinical syndrome characterized by a decreased ability to respond to stressor events and a state of vulnerability, as a consequence of cumulative physiological decline and accumulating co-morbidities [10]. Decline from fitness to frailty occurs due to various factors such as sarcopenia, chronic inflammation, impaired metabolism leading to acidic state, vitamin D deficiency and cellular senescence [11–15]. Within the general population, frailty status has been shown to have significant associations with adverse outcomes, including falls, hospitalization, reduced health-related quality of life and mortality [10]. The FRAIL scale (a 1 to 5 scoring system based on presence of five self-reported items: fatigue, resistance, ambulation, illness and loss of body weight), a frailty phenotype model of assessment, is useful to identify components of physical frailty—including unintentional weight loss, handgrip strength, self-perceived exhaustion, walking speed and physical activity [16,17].

The relationship between frailty status and increased risk of urolithiasis has only begun to be explored recently. Given patients with diabetes mellitus are known to be at greater risk of developing urolithiasis, Chao et al. [18] investigated whether frailty status is independently associated with incidence of urolithiasis amongst those diagnosed with diabetes mellitus. This population-level cohort study was retrospectively performed using data from the Longitudinal Cohort of Diabetes Patients (LCDP) database in Taiwan between 2004 and 2010, where patients were followed up until they developed urolithiasis. Frailty status was measured using a modified and validated version of the FRAIL scale. Amongst 525,368 diabetic patients, results derived from Cox proportional hazard regression analysis showed that diabetic patients fulfilling at least one FRAIL criterion were significantly at greater risk of urolithiasis compared to patients who fulfilled none or only one of the FRAIL criteria (for 2 FRAIL criterion: HR 1.23, 95%CI 1.12–1.35, for ≥3 FRAIL criterion: HR 1.45, 95%CI 1.12–1.89). Despite the statistical associations shown between these two conditions, it remains debatable whether a causative relationship between frailty status and a disease such as urolithiasis could exist.

How a more severe frailty status is associated with greater risks of developing urolithiasis has been postulated, nevertheless. Compared to those who are considered non-frail or living with mild frailty, older individuals living with moderate and severe frailty may be prone to a sedentary lifestyle, with prolonged bed rest and gradual decline of their ambulatory function. Reductions in physical activity and mobility are recognized as significant risk factors of hypercalciuria, and patients have poor clinical outcomes as a consequence of increased calcium-based urinary stone formation [19]. As a consequence of a sedentary lifestyle, obesity (defined as body mass index > 30 kg/m$^2$) has emerged as a prevalent public health issue in the elderly population, and a good prognosticator of frailty-associated outcomes in older people [20,21]. Obesity is demonstrated as a risk factor for the formation of calcium oxalate and uric acid stones in the elderly, according to findings from comprehensive cohort studies such as the Amirkola Health and Ageing Project (AHAP) [22]. Chronic immobility also affects bone metabolism, with increased bone turnover eventually leading to a state of resorptive hypercalciuria [23]. Another explanation for increased risks of developing urolithiasis amongst older and frail individuals likely relates to their dietary patterns. The frail and elderly are usually encouraged to increase their dietary protein intake due to sarcopenia [24]. Increased intake of dietary products rich in animal protein in the older population heightens their risk of hyperoxaluria and hypercalciuria [25]. This association is explained by increased acidic production during metabolic breakdown of dietary proteins, which enhances the processes of oxalate excretion, bone mineral mobilization and intestinal calcium absorption. These metabolic changes elevate the glomerular filtration rate and encourage calcium oxalate stone formation [26]. The build-up of urolithiasis in older people is also greater due to decreased fluid intake and delayed signalling of thirst, leading to dehydration [27]. A considerable number of elderly and frail individuals live with some degree of cognitive impairment, which affects their ability to identify fluid intake needs [28]. Dehydration is considered one of the most important risk factors of urolithiasis. In most instances, the state of dehydration
increases urinary supersaturation of calcium oxalate, and subsequently hastens the process of urinary stone formation [29]. Less common types of urinary stones, such as carbonate apatite stones, have greater prevalence with advancing age according to epidemiological studies [30]. This trend is likely explained by the increased number of old and frail individuals living with hypercalciuria. Historically, there is evidence suggestive of a longitudinal relationship existing between aging and urine acidification [31]. Recent evidence propose that urine acidification may also be associated with frailty status [18]. Urine acid stone formation as a consequence of urine acidity may be inherited, or associated with excess dietary protein intake [32]. Another potential source of increased risk of urolithiasis in old and frail individuals relates to their susceptibility of having recurrent urinary tract infections (UTIs) [33]. More commonly observed in postmenopausal women and institutionalized patients, urease-positive recurrent UTIs predispose to the build-up of ammonia and alkaline urine, and eventual formation of struvite and carbonate apatite crystals [34,35]. These crystals will then deposit themselves in the urinary tract, and lead to a state of infection-induced urolithiasis [35]. Another factor for increased urolithiasis risk in the elderly population may relate to low urinary citrate excretion, due to dietary patterns and age-associated decline in renal clearance and metabolic regulation of acid–base balance. Low urinary citrate excretion is a known risk factor for the development of urolithiasis in adults [36]. An alkaline agent, citrate inhibits urinary stone formation by forming complexes with calcium within the urinary tract, and inhibits spontaneous nucleation, as well as the growth and agglomeration of crystals [37]. Further evidence is required to clarify whether older and frail individuals are more susceptible to low urinary citrate excretion.

Multidisciplinary support to apply prevention strategies in primary care may be useful to identify risks early and reduce the incidence of urolithiasis. Exercise programs designed for the elderly can encourage increased physical activity in older people, whilst falls risks could also be monitored [38]. As advocated by conclusions from the Women’s Health and Aging Studies (WHAS), Survey of Health, Ageing and Retirement in Europe (SHARE) and the Study on Global AGEing and Adult Health (SAGE), regular family support and dietician input are helpful to ensure a balanced fluid and food intake regime in the elderly population [39–41]. This could be achieved whilst accounting for the older individual’s fluid and nutritional needs and risks of urolithiasis, UTIs as well as other co-morbidities [42]. Although many food sources that benefit other nutritional areas also present high amounts of oxalate, the impact of high oxalate levels could be mitigated if meals and snacks are accompanied by additional fluids and calcium supplementation to diminish oxalate absorption, and to reduce urinary supersaturation of calcium oxalate [43,44]. Measures to improve hygiene in an older person’s living and sanitary environment should be encouraged at all times to reduce the risk of frequent UTIs. For older people living with moderate to severe frailty but without adequate family or social support, regular general practitioner and community geriatrician review is important to ensure primary prevention strategies are being adhered to as much as possible [45]. This will particularly be the case for institutionalized patients and patients with cognitive impairment. The use of citrate supplements as a prophylactic measure has demonstrated positive effects on reducing the formation of calcium oxalate and other calcium-based urinary stones within the general adult population, including old and very old individuals [44].

In summary, we hope our focused commentary can bring greater awareness to the scale and significance of this issue going forwards. More work is required to determine the significance of associations between frailty status and incidence of urolithiasis within the general geriatric population. Further research initiatives to optimize prevention strategies are also anticipated to ensure the incidence of urolithiasis could be maintained to the minimum for our patients living with frailty.

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