

EDITORIAL

FRAILTY AND POLYPHARMACY

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Frailty is now recognized as a major risk factor for future disability and mortality (1-3). The physical frailty phenotype as originally defined by Fried et al (4) has been simplified to be rapidly detected using either the FRAIL screen (5-7) or the Gerontopole Screening Questionnaire (8, 9). The FRAIL scale has been shown to have equivalent predictive ability to other more complex frailty scales (10, 11). Polypharmacy related to the increase in illnesses in older persons has been identified as one of the treatable components of the FRAIL scale (12). An alternative approach to defining frailty has been proposed by Rockwood (13). This scale consists of adding up all the deficits a person has and presenting the result as a percentage of all deficits measured. In actuality, this represents a co-morbidity index. Other frailty scales such as the Tilburg Frailty Indicator (14, 15) and the Groningen Frailty Index (16,17) include both physical and psychosocial elements. Recently, a number of studies have suggested that the presence of a cognitive deficit leads to worse outcomes in persons with a physical frailty deficit (18-20).

It is now well recognized that polypharmacy in older persons leads to poor outcomes (21-24). Six cross-sectional studies have suggested that the presence of polypharmacy is significantly related to an increased propensity for older persons to have the physical frailty phenotype (25-30). These studies have suggested a reasonable cut-off for polypharmacy's relationship to frailty is more than 6 medicines.

There are numerous reasons why polypharmacy may lead to frailty (31). Anticholinergic (atropinic) drug exposure has been shown to be associated with frailty (32). In frail nursing home residents anticholinergic drugs are associated with increased functional decline, more falls and a greater incidence of dementia and delirium (33-35). Stopping anticholinergic drugs improves cognitive function (36, 37). Anticholinergics are also associated with hip fractures (38). Another study found that anticholinergic drugs decreased the ability to bathe, groom, dress, transfer and to be mobile, as well as increasing in-hospital mortality (39). It should be pointed out that one recent study showed that appropriate anticholinergic medication use may be relatively safe in hospitalized patients (40). Weight loss is common in older persons (41-43). Loss of fat results in more side effects from fat soluble drugs. In addition, persons with weight loss tend to have a decline in their blood pressure. Thus, older persons are often overtreated for hypertension by not having their antihypertensive medicines reduced (44,45). Dehydration is common in older persons and is often made worse by inappropriate use of diuretics to treat pedal edema

(46). Dehydration is associated with frailty, falls, syncope, poor cognition, disability and mortality (47-51).

Changes in metabolism and clearance of drugs with aging increases the chances of drug toxicity and drug-drug interaction (52, 53). The decrease in L-thyroxine clearance with aging often results in excess L-thyroxine doses which lead to weight and muscle loss, osteoporosis and heart disease. The use of selective serotonin reuptake inhibitors (SSRIs), can lead to hyponatremia and delirium (54). Proton pump inhibitors (PPIs) are overused in older persons, leading to reduced vitamin B12 and calcium absorption and possibly bacterial overgrowth and clostridium difficile infections (55). In geriatric wards and nursing homes PPIs are associated with increased mortality (56). Overtreatment of persons with diabetes mellitus is associated with frailty (57-59). Overall, polypharmacy has been associated with a reduction in walking speed and gait strength, disability and mortality (60-64). Polypharmacy is also related to cognitive decline and delirium (65-67). Persons with cognitive decline have decreased self-management skills and this creates increased risks when they are on multiple medications (68). Reduction in polypharmacy leads to reduction in costs without creating any increase in harms (1, 69-71). We recommend that all frail older persons have their medications reviewed by a pharmacist with the ideal of reducing medications to 6 or less (72). While this may not be possible in every individual, we believe that it is possible in the majority of frail older persons. If no pharmacist, either the STOPP/START or Beers criteria can be used (73, 74). The "Fit for the Aged" (FORTA) is a system developed in Germany that appears to have some additional advantages in being easy to use in older persons (75). It also needs to be recognized that polypharmacy is a major cause of non-adherence to drug therapy (76).

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FRAILTY AND POLYPHARMACY

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