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Original Study

Exposure to Atropinic Drugs and Frailty Status

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A B S T R A C T

Background: Atropinic drugs can increase the risk of falls, cognitive impairment, and mortality in older patients; however, whether exposure to atropinic drugs is associated with frailty status remains unknown. Our aim was to assess the association between frailty status and exposure to atropinic drugs in a geriatric day hospital population.

Methods: We carried out a cross-sectional study that included all the patients consulting for the first time at the Geriatric Frailty Clinic for Assessment of Frailty and Prevention of Disability in Toulouse, France, from January 2013 to October 2013. Frailty was defined by 3 or more of Fried et al's criteria. Atropinic drugs were those with clinical antimuscarinic effect from the Anticholinergic Drug Scale (excluding drugs weighted 1 point and not listed by Durán et al) and from Laroche et al list (to include drugs marketed in France not present in the Anticholinergic Drug Scale). To explore a dose-effect relationship, we calculated the atropinic burden using the Anticholinergic Drug Scale weights. We performed logistic regression models adjusted for age, gender, comorbidities, being community dwelling or not, cognitive status, educational level, and polypharmacy (≥6 drugs).

Results: We included 437 patients (227 frail and 210 robust or prefrail). Exposure to at least one atropinic drug was associated with frailty (odds ratio 1.97, 95% confidence interval 1.10–3.53, $P = .02$). Due to a statistically significant interaction between age and atropinic burden, a dose-effect relationship for atropinic burden was explored in patients younger than 85 years, showing a significant association between atropinic burden score and frailty ($P = .01$). The Odds ratio for an atropinic burden greater than or equal to 3 versus 0 was 3.84, 95% confidence interval 1.43–10.34 ($P < .01$).

Conclusions: In a geriatric day hospital, population frailty is associated with a high atropinic burden.

Frailty predicts various adverse events, including falls, delirium, and functional decline.[1–4] Atropinic drugs also have been reported to increase the risk of falls,[5,6] hip fractures,[7] cognitive impairment,[6,8–11] and mortality. Atropinic drugs are listed among the potentially inappropriate drugs in older patients[12,13] but they remain regularly prescribed especially in older patients.[14–16] Whether exposure to atropinic drugs is associated with frailty status is unknown. The aim of this study was to assess the association between frailty status and exposure to atropinic drugs in a geriatric day hospital population.

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Methods

Patients

We carried out a cross-sectional study that included all the patients consulting for the first time at the Geriatric Frailty Clinic for Assessment of Frailty and Prevention of Disability in Toulouse University Hospital, France, between January 2013 and October 2013. Procedure of recruitment of this population of frail older people has been previously reported in detail.[17] Briefly, the aim of this clinic is to detect frailty or prefrailty among patients older than 65 years referred by their general practitioner and organize a program of care to prevent disability.[17]

A standardized assessment of comorbidities, place of dwelling, cognitive status (Mini-Mental Status Examination [MMSE]), educational level (illiterate, elementary school, middle school, high school, undergraduate/postgraduate), and exposure to drugs (drug name and dosage) is completed and prospectively computerized for all patients. It is performed by a trained geriatric nurse and a geriatrician.[17] Frailty status also is defined for all patients by using was Fried et al's criteria. These include (1) shrinking (unintentional weight loss of $\geq$10 pounds in previous year or, at follow-up, of $\geq$5% of body weight in previous year), (2) weakness (grip strength in the lowest 20% at baseline, adjusted for gender and body mass index), (3) poor endurance and energy (self-report of exhaustion), (4) slowness (based on time to walk 15 feet, adjusting for gender and standing height), and (5) low physical activity level (weighted score of kilocalories expended per week).[18] Patients were frail if they had 3 or more criteria, prefrail if they had 1 or 2, and robust if they had none.

Exposure to Atropinic Drug and Atropinic Burden Scoring

We used the Anticholinergic Drug Scale (ADS).[19] In this scale, each drug has a score ranging from 0 to 3 depending on the intensity of its antimuscarinic effects. However, this list includes drugs with affinity for muscarinic receptors in vitro without clinical atropinelike effect (scored 1 point, eg, furosemide, prednisolone, and captopril). As we wanted to consider only the atropinelike drugs that have a clinical antimuscarinic[20] effect, we excluded from the ADS the drugs scored 1 point in the ADS because of potential antimuscarinic effects in vitro but without clinical antimuscarinic effect (ie, the drugs not listed by Durán et al in 2013).[21] Last, because some atropinic drugs marketed in France are not listed in the ADS, we added the drugs with a clinical atropinic effect listed by Laroche et al.[13] Exposure to atropinic drugs was defined by exposure to at least one of these drugs. We included topical forms. Drug exposure was recorded based on prescription lists provided by general practitioners and questioning of the patient and relatives accompanying the patient.

To assess a dose-effect relationship, we calculated the atropinic burden score (ABS) for each patient. We attributed to atropinic drugs the corresponding score of the ADS.[19] For drugs marketed in France not listed in the ADS, a college of pharmacologists attributed an atropinic weight, as used in a previous French study.[14]

The included drugs with their corresponding atropinelike scores are listed in the Appendix.

Statistical Analyses

The study population was split in 2 groups: the group of frail patients and the group of prefrail or robust patients. Comparisons between the 2 groups used χ^2 or the Fisher test for qualitative variables, and t test or Wilcoxon-Mann-Whitney test for quantitative variables. We performed a model of logistic regression to assess the association between frailty status and exposure to atropinic drug, and then between frailty status and ABS, categorized in 0, 1 to 2, and 3 or more (reference group: ABS = 0). We choose the value of 2 as the cutoff because the mean ABS in the general population was 1.8 in the previously quoted French study.[14] Analyses were adjusted for age, gender, cognitive impairment (MMSE <24), institutionalization (yes vs no), educational level (illiterate, elementary school, middle school, high school, undergraduate/postgraduate), comorbidities (using the Charlson score categorized as 0, 1–2, 3–4, and $\geq$5),[22] and polypharmacy. The threshold of at least 6 drugs defined polypharmacy, as previously demonstrated in this population.[23] All the variables significantly associated with frailty at the threshold of 20% in univariate analyses were included in the multivariate models (backward procedure, α = 5%). Statistical analyses were carried out using SAS V9.4 software (SAS Institute, Inc., Cary, NC).

Results

Study Population

Among the 511 patients hospitalized at the Geriatric Frailty Clinic for Assessment of Frailty and Prevention of Disability during the study period, 437 patients were included for analysis (Figure 1). Of

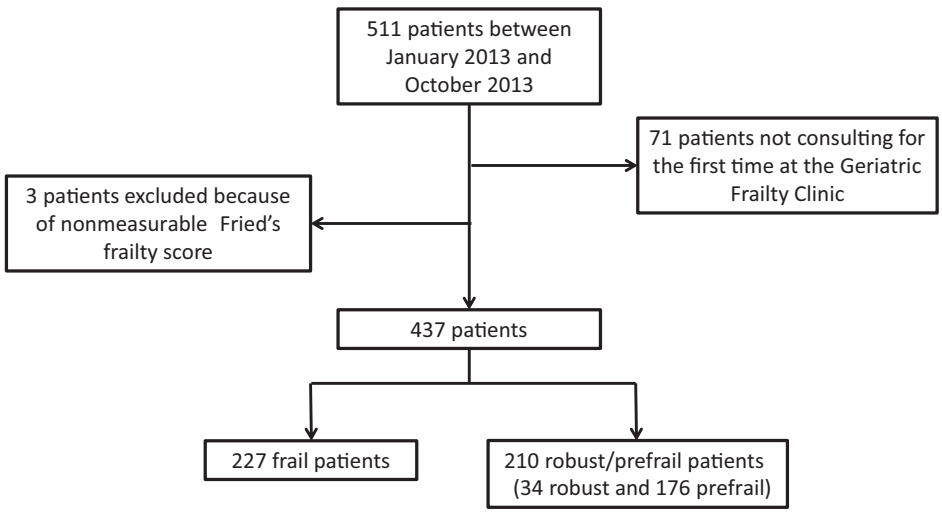

Fig. 1. Flowchart illustrating the selection of the patients.