

NEW PAPERS

When and how to reduce antihypertensive treatment in nursing home residents: results of the RETREAT-FRAIL trial



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Very old patients consume a large number of medications, especially those intended for the prevention or treatment of cardiovascular (CV) diseases. Since hypertension is the most common risk factor in people over 80 years of age, with a prevalence reaching more than 70%, most people in this age group receive chronic antihypertensive drugs, which have demonstrated, in randomized clinical trials (RCT), substantial benefits in the prevention of cardiovascular complications.^{1,2} However, RCTs generally exclude the very old and the frailest patients, who are more likely to experience adverse effects of antihypertensive drugs.³ Thus, the population habitually consuming several of these drugs has always been excluded from randomized clinical trials that have evaluated the benefits and risks of these treatments. On the other hand, numerous observational studies indicate that in old frail patients, low blood pressure (BP) is associated with higher CV morbidity and mortality, particularly in the presence of antihypertensive treatment.^{4,5} These observations raise major questions regarding the management of hypertension in frail old patients.⁶ Recent European guidelines on the management of hypertension^{7,8} emphasize the need to establish BP targets and therapeutic strategies according to the level of frailty, and to consider gradual reduction of antihypertensive treatment in frail older patients with low BP. However, evidence on the benefit/risk ratio of drug deprescription in these patients is currently very limited.

We designed and conducted the RETREAT-FRAIL RCT to answer these questions: Is the increased mortality in frail older patients with low BP on

multiple antihypertensive therapy reversible by reducing antihypertensive treatment? What are the benefits and risks of reducing antihypertensive treatments in these people with high CV risk?

RETREAT-FRAIL was a multicenter RCT in nursing home (NH) residents in France, aged 80 years and older, treated with more than one antihypertensive drug and with a sitting systolic BP (SBP) below 130 mmHg. 1048 patients from 108 nursing NHs were randomized to either a gradual step-down of antihypertensive treatment strategy (intervention group, n=528) or usual care (control group, n=520). Before randomization, we thoroughly reviewed the clinical status of the patients to determine the indications for each antihypertensive drug administered. Only drugs without compelling indications could be discontinued in patients randomized to the step-down strategy. To include even the most frail patients, the only exclusion criteria applied were patients without any antihypertensive drug that could be discontinued due to compelling indications and patients with a life expectancy of less than 3 months. Also, the ethics committee allowed family members or other close relatives to give informed consent when a patient was unable to consent themselves. Clinical follow-up of both groups took place in the NHs where they resided, at a regular pace (every month for the first six months, then every two months) and was identical for both groups, except for the reduction in antihypertensive treatment applied only to the intervention group. The first subject was randomized on April 15, 2019, and the last on July 1, 2022. The recruitment period was extended by one year compared to the initial



schedule, mainly due to the COVID-19 pandemic. Follow-up ended in July 2024, two years after the inclusion of the last patient.

Analysis of the initial characteristics of the 1,048 randomized patients confirmed the specificities of this population: an average age of 90 years, composed mainly of women (80%), taking on average more than 9 different medications per day, of which 2.5 were cardiovascular (more than 3 if antidiabetic and lipid-lowering drugs are included). According to the Clinical Frailty Scale score⁹, nearly 40% of these subjects presented severe to very severe frailty and less than 10% were fit or doing well. The population treated for hypertension also had a heavy cardiovascular history: nearly 40% with atrial fibrillation, 24% with heart failure, 19% with a history of stroke and 19% with coronary artery disease. More than 23% were treated for diabetes. This population is very representative of the 700,000 subjects over 80 years old living in NHs in France, but also of many other older people living at home with a loss of autonomy, cognitive impairment, mobility problems, and related difficulties, needing continuous assistance for most daily activities.

The primary endpoint was all-cause mortality. Secondary endpoints included major adverse cardiovascular events, systolic BP (SBP) levels, number of antihypertensive medications, functional status, falls, fractures, quality of life, non-cardiovascular deaths, and COVID-19-related deaths. During a median follow-up of 38.4 months, the number of antihypertensive medications was reduced from a mean of 2.6 to 1.5 in the step-down strategy group and from 2.5 to 2.0 medications in the usual care group. The between-group difference in SBP throughout the follow-up period was 4.1 (1.9-5.7) mmHg. All-cause mortality was observed in 61.7% of patients randomized in the step-down strategy and in 60.2% of patients in usual care [HR: 1.02 (0.86-1.21), $p = 0.78$]. The step-down strategy tended to be more beneficial on all-cause mortality in the frailest patients (interaction between step-down strategy and frailty level, $p = 0.08$). Changes in autonomy, cognitive function, muscle strength, gait, and quality of life were not different in the two treatment groups, as well as, non-cardiovascular mortality, falls, fractures, and other serious adverse events. A lower number of

COVID-19-related deaths was observed with the step-down strategy (1.1% vs. 3.1%).

In summary, in NH residents aged over 80 years, with a SBP less than 130mmHg, the deprescribing strategy resulted in a long-term reduction in the number of antihypertensive medications compared to usual care, resulting in a slight but significant increase in BP without changes in morbidity, mortality, functional status, or adverse effects. These results show that deprescribing antihypertensive treatments is possible subject to a thorough assessment of the clinical condition of patients and regular monitoring, in the same way as when prescribing a medication.

In conclusion, RETREAT-FRAIL is the first clinical trial demonstrating that deprescribing antihypertensive drugs does not increase mortality, morbidity or other adverse effects. This strategy could therefore be considered in very old subjects with low blood pressure levels, particularly the most frail, in whom polymedication constitutes a major problem.

*The main results of this study have been published here: A. Benetos, S. Gautier, A. Freminet et al. Reduction of Antihypertensive Treatment in Nursing Home Residents. *N Engl J Med*. 2025 Aug 29. doi: 10.1056/NEJMoa2508157. Online ahead of print. PMID: 40879421

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