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# Frequency of hypertension in hospitalized population with osteoporotic fractures: Epidemiological retrospective analysis of Hospital Discharge Data in the Apulian database for the period 2006–2010

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## Abstract

Osteoporosis and hypertension are two widespread diseases, which share many of the same risk factors such as advanced age, early menopause, smoking, and physical inactivity. The aim of this study is to examine the association between fragility fractures, anti-hypertensive drugs (subgroup C02, according to the Anatomical Therapeutic Chemical classification system [ATC]), diuretics (subgroup C03), b-blocker (subgroup C07), calcium antagonist (subgroup C08) and renin-angiotensin-aldosterone system regulator (subC09), and drugs administration for osteoporosis among the osteoporotic population of a region of Southern Italy.

We retrospectively studied "Hospital Discharge Data" (HDD) in the Apulian database for the period 2006–2010 to find fragility fractures treated with hospitalization in men aged over 65 years and in women aged over 50 years. We then checked the database for drug prescriptions to identify those patients who had taken at least one osteoporosis drug. Within this latter group, based on hospital admissions and prescription records, we identified the patients affected with hypertension.

We observed that, between 2006 and 2010, in Apulia, 177,639 patients were hospitalized and diagnosed as having fragility fractures. The prevalence of hypertension patients in Apulia in this period was estimated at 44.3%. In the same region and period, the prevalence of patients with fragility fracture, who also had hypertension, was 80.9%. The percentage of fracture was lowest in the female population aged 50–59 years (52.5%), while the highest was in women aged > 80 years (92.5%). We observed that in hypertensive patients the most frequent site of fracture was the femur (43,638 cases), while the least frequent were the tarsus and metatarsus (742 cases combined). The patients who took angiotensin-converting enzyme (ACE) inhibitor and diuretic drugs presented a higher number of fragility fractures, while the calcium antagonists, beta-blockers, and ATC anti-hypertensive drugs were linked to a reduced incidence of lesions.

Hypertension is associated with increased fracture risk in the Apulia population. The bone demineralization effect of this disease should be taken into account during the management of these patients. The different distribution of fragility fractures in relation to anti-hypertensive treatment warrants further investigation.

## Keywords

drug, epidemiology, hypertension, osteoporosis

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## Introduction

Osteoporosis and hypertension are two frequent diseases among the aging population and they often co-exist.[1] High blood pressure leads to increased loss of calcium in the urine and increases movement of calcium from bone. Hypertension also causes high levels of parathyroid hormone, which accelerate bone turnover, decreasing bone mass.[2] In addition, calcium loss related to hypertension may be due to a defect in the kidney's ability to handle calcium. Finally, increased angiotensin II levels in hypertensive patients have a harmful effect by increasing bone resorption and inhibiting mineralization.[1]

Medications used for the treatment of hypertensive pathology have been shown to modulate bone health in both a positive and/or negative manner. On one hand, thiazide diuretics can improve the osteoporosis by ameliorating the detrimental effects of high blood pressure as well as the direct effects on bone.[1] Thiazides reduce sodium reabsorption, and increases urinary loss of sodium and calcium.[3] On the other hand, angiotensin-converting enzyme (ACE) inhibitors block release of the mediators which activate osteoblasts, decrease blood flow in bone marrow capillaries and drop in free calcium ion levels in plasma while increasing parathormone (PTH).[4] Beta-blockers have an effect on bones related to the role of the sympathetic nervous system in the regulation of bone metabolism, inhibiting both anabolic and catabolic actions on bones.[5] Calcium channel blockers reduce secretion of osteocalcin and inhibit PTH-stimulated takeover of calcium in osteoblasts.[6] Loop diuretics increase calcium leak in kidneys, level of PTH, and 1,25(OH)2D in plasma.[4]

The main aim of this study is to investigate the prevalence of hypertension in a more numerous population of patients with known osteoporosis and fragility fractures treated with hospitalization and living in a region of Southern Italy. Furthermore, we aim to verify if there exist a direct influence of anti-hypertensive drugs on the onset of fragility fractures.

## Materials and methods

### *Patients*

We designed a retrospective observational clinical study. We carried out a survey of patients referred to the orthopedics departments of major hospitals in a Southern region of Italy (Apulia) which has a population of 4,090,266 [ISTAT Data, updated 31-12-2013]. We screened the "Hospital Discharge Record" (HDR) database in the period 2006–2010 in order to identify patients with a new fragility fracture diagnosis requiring hospitalization. For our study, we selected male patients aged over 65 years (to study osteoporosis caused by senescence) and female patients aged over 50 years (to assess postmenopausal osteoporosis) whose HDR reported domestic accident in the item "trauma" and were not recorded in the "deceased" list. The Local Ethical Committee approved the study. Indeed, the absence of specific codes for fragility (mainly osteoporotic) fractures results in a lack of perception of fracture burden, leading to problems in as exact evaluation of osteoporotic fractures in the elderly. We also checked the database of drug prescriptions to reach the people who assumed one of the drugs for osteoporosis and calcium and vitamin D integrator.

We cross-checked the database of patients affected by fragility fractures with the osteoporosis drug prescription database using individual health codes eliminating all repetitions. This database represents the prevalent population of the study.

The proportion of the patients admitted for fragility fractures who were also being treated for osteoporosis and hypertension was the main study outcome. This was ascertained carrying out data linkage between prevalent population and HDA and drugs prescription database. In particular, a hypertensive patient was defined as:

- a patient belonging to the prevalent population whose admission was related to hypertension (ICD9CM 401-405 code),

- a patient with at least one prescription for anti-hypertensive drugs (ATC anti-hypertensive – C02, diuretics – C03, beta-blocker – C07, calcium antagonists – C08, renin angiotensin drugs – C09) verified by data linkage with the regional prescription database.

The data were stratified into decades of age (50–59 years, 60–69 years, 70–79 years, and > 80 years) and between gender (male and female).

## Results

In the period 2006–2010, we observed that in Apulia, 177,639 patients were admitted for fragility fracture and, compared with each year, 2006 had the highest percentage (34.7%), while the trend progressively decreased to 15.5% in 2010. The analysis of the admission data for fragility fracture in relation to stratification of age showed that the incidence was highest in the 70–79-year-old age group (64,917 fractures) and lowest in the 50–59-year-old age group (17,260 fractures). The fragility fractures were more common among women (41,943 fractures) compared to men (1867 fractures). The sites most affected were the proximal femur, humerus, wrist/forearm, lumbar spine, tibial pilon, and dorsal spine.

In the prevalent population, we identified 143,707 patients (80.9%) who had hypertension and/or assumed hypertensive drugs (Tables 1–3). This value showed an increase in relation to age, from 52.5% in the 50–59-year-old age group to 92.2% in the patients aged over 80 years (Table 2); the data moreover showed a greater prevalence of hypertension in the male population with fragility fracture (85.4%) compared to the female population (80.4%) (Table 3). The patients with fragility fracture and hypertension under treatment mostly had femur fractures (43,638 fracture), which is in accordance with the trend of the osteoporotic Apulian population. The main class of drugs used in our study group was renin-angiotensin-aldosterone inhibitors, followed by diuretics, calcium antagonists, beta-blockers, and anti-hypertensive drugs (Table 3). This distribution does not perfectly overlap that of the general Apulian population who used mainly renin angiotensin regulator, followed by beta-blockers, diuretics, calcium antagonists, and anti-hypertensive drugs.

**Table 1.** Stratification of the Apulian population affected by hypertension: the incidence was highest in the 70–79-year-old age group and among women.

| Age group (years) | M | F | **Total** |
|---|---|---|---|
| 50–59 | – | 9066 | 9066 |
| 60–69 | – | 29,648 | |
| 65–69 | 1379 | – | 31,027 |
| 70–79 | 6656 | 49,333 | 55,989 |
| > 80 | 6221 | 41,404 | 47,625 |
| Total | 14,256 | 129,451 | 143,707 |

**Table 2.** The percentage of patients affected by fragility fracture and hypertension diagnosis according to gender: the incidence was highest in the 80–89-year-old age group and among women.

| Age group (years) | M | F | **Total** |
|---|---|---|---|
| 50–59 | – | 52.53% | 52.53% |
| 60–69 | – | 70.69% | |
| 65–69 | 73.86% | – | 70.82% |
| 70–79 | 84.01% | 86.56% | 86.25% |
| 80–89 | 90.12% | 92.53% | 92.21% |
| Total | 85.40% | 80.43% | 80.90% |

## Discussion

This study aimed to measure more appropriately the influence of the risk factor of hypertension in the Apulian population affected by fragility fractures. In the Apulian population with fragility fractures, the presence of co-mobility is high: 66% have cardiovascular diseases, 44% have rheumatic diseases, and 21% have diabetes.[7–9] Hypertension has been postulated as a risk factor for fractures and the relationship is likely independent of bone mineral density (BMD). In a previous Serbian study, around 61% of patients with osteoporosis also were affected by hypertension.[10] The results of our study confirm the correlation between osteoporosis and hypertension demonstrating that 44.3% of the Apulian population aged over 50 years is affected by hypertension. This percentage tends to increase significantly among patients being treated for osteoporosis who had had a fragility fracture which had necessitated hospitalization (reaching 80.9%). From the data examined, there emerged a gender difference with regard to age. Between 50 and 70 years, the fragility fracture and osteoporosis incidence was higher among men while over the age of 70 years, it was more frequent among women. The most frequently affected site of fragility fracture was the proximal femur. This finding suggests that the condition of hypertension may have a greater demineralization effect on the cortical bone with respect to the trabecular bone.[11] In the analyzed Apulian population hospitalized for fragility fracture and in treatment for osteoporosis, the most common class of drugs used for hypertension were ACE inhibitors and diuretics, followed by calcium antagonists, beta-blockers, and anti-hypertensive drugs. Also, in the general Apulian

**Table 3.** The drug class and fragility fracture according to sites: the most given drug was renin-angiotensin-aldosterone inhibitor in patients affected by femoral fracture.

| Type of fracture | Drug class | | | | |
|---|---|---|---|---|---|
| | Anti-hypertensive | Beta-blocker | Calcium antagonist | Loop renal and thiazide diuretics | Renin angiotensin/ Aldosterone inhibitors |
| Spine | 523 | 1511 | 1816 | 2740 | 3689 |
| Humerus | 607 | 1407 | 1798 | 2666 | 3612 |
| Forearm | 406 | 1148 | 1342 | 1826 | 2855 |
| Femur | 2275 | 5331 | 7772 | 13,296 | 14,964 |
| Tibial pilon | 310 | 906 | 1013 | 1359 | 2105 |
| Tarsus/ metatarsus | 38 | 129 | 128 | 172 | 275 |

population, the most commonly used drugs were ACE inhibitors and diuretics followed by calcium antagonists, beta blockers, and anti-hypertensive drugs. Although preliminary results of our study suggest that diuretics may have a demineralization effect and that beta-blockers and calcium antagonists may reduce risk fracture, the literature has not identified a correlation between the administration of anti-hypertensive drugs and osteopenia effect.

## Conclusions

In conclusion, it seems fundamental to insert in the treatment protocols of hypertension, the clinical and densitometry evaluation of osteoporosis.

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