Uncontrolled hypertension in primary care

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ABSTRACT

Background. The aim of the study was to assess the prevalence of uncontrolled hypertension and its characteristics in comparison with controlled hypertension.

Material and method. 3,145 hypertensive patients from 19 family medicine practices of Timiș County were evaluated from 2010 to 2014 clinically and by laboratory.

Results. After 12 months of monitoring, 1008 patients (32.05%) had controlled hypertension and 2137 (67.95%) had office BP ≥ 140/90 mmHg, being considered uncontrolled. ABPM was performed in 690 patients with uncontrolled hypertension and it allowed to diagnose a “white-coat” effect in 34.18% of them, as they had normal blood pressure values recorded with ABPM. Abnormal values were found in 520 (65.82%), of which 360 (69.23%) were uncontrolled by treatment, 85 (16.35%) were untreated, 42 (8.08%) had resistant hypertension and 33 (6.34%) secondary hypertension. The most common causes of uncontrolled hypertension were: poor adherence to treatment, inadequate doses and combinations, excessive salt consumption, obesity, metabolic syndrome, secondary and resistant hypertension. Compared with controlled hypertension, uncontrolled hypertensive patients were more often older, presented more severe and long hypertension evolution, organ damage and cardiovascular complications.

Keywords: uncontrolled hypertension, diagnosis, primary care

BACKGROUND

In clinical practice, uncontrolled hypertensive patients represent a frequent and serious problem. In spite of a better access of the population to medical care, the prevalence of uncontrolled hypertension is increasing, being the result of an aging population, of the growing prevalence of obesity and other comorbidities as metabolic syndrome, diabetes mellitus and chronic kidney disease (1).

Defining the clinical characteristics of patients with untreated hypertension, inadequately treated, secondary hypertension and treatment true resistance will ameliorate the strategies and interventions for improving management of hypertension. Significant factors in defining accurately uncontrolled hypertension impose exclusion of BP measurement artifacts, of “white-coat” effect, evaluation of drug combinations and doses, analysis of co-medication and of adherence to treatment. The evaluation of characteristics of uncontrolled hypertensive patients may improve in future blood pressure control and reduce morbidity and mortality caused by hypertension (2).

The objectives of the study were:

- To evaluate the incidence of uncontrolled hypertension in primary care settings after 1 year of surveillance.
• To analyze the clinical and ABPM variables associated with uncontrolled, compared with controlled HT.
• To detect the etiology and lifestyle factors contributing to uncontrolled hypertension.
• To evaluate the cardiovascular risk, organ damage and comorbidities of uncontrolled hypertension.

**MATERIAL AND METHODS**

From a number of 5210 hypertensive patients from 19 family medicine offices of Timiș county, evaluated during 2010-2014, 3145 had at least 2 visits at their family doctor (at the entry in the study and after 12 months). The database of the patients included demographical and clinical variables as cardiovascular risk factors, target organ damage, cardiovascular events, office BP measurements, 24-h ABPM and therapy. The control of hypertension was evaluated after twelve months from study entrance. All patients received at their first encounter recommendations for lifestyle changes and medical therapy in 2895 cases (92.05%).

Hypertension was defined as SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg and/or a positive response to the question: “Are you currently on medication to lower BP?” Control of hypertension was defined as BP < 140/90 mmHg across all 12 months survey controls. Awareness of hypertension was determined by the affirmative response to the question: “Have you ever been told by a doctor or other healthcare provider that you had hypertension?” Treatment of hypertension was established by responding “yes” to the question: “Because of your high blood pressure, are you taking prescribed medicine now?”

Uncontrolled hypertension was defined as blood pressure ≥140/≥90 mmHg, when subjects reported lifestyle changes and in the majority of cases medication consisting of ≥1 antihypertensive drug. Resistant hypertension (RHT) was considered present in patients treated with at least 3 antihypertensive agents, including a diuretic, at optimal doses or maximal tolerated, with office blood pressure (OBP) that exceed the target values of 140 and/or 90 mmHg.

All family doctors implied in the study were instructed to use the same method of BP measurement and patient evaluation. Office BP readings were calculated as the average of the second and third reading (the first reading was not taken into account), performed in the office in the morning at 2516 patients (80% of cases), and at 629 patients (20%) during the afternoon. The measurements were made with a calibrated aneroid sphygmomanometer Riester R1 in 2202 patients (70.01%), or using a semi automatic calibrated sphygmomanometer Omron M3 in 943 patients (29.99%).

MATA was performed with BTL-08 ABPM devices, 4 measurements/h were scheduled during the daytime and 2 measurements/h during the nighttime. The patients were advised to perform their usual daily activities, to hold still their extended arm during cuff inflations and to keep a daily diary with their activities and time of drug administration. ABPM was considered valid if 80% good measurements were obtained (1).

The antihypertensive medication administered to the patients was based on the clinical experience of family doctors and on the pathophysiological mechanisms involved in hypertension. The COMBAT courses of Romanian Society of Hypertension and the teachers of the Department of Family Medicine of the University of Medicine and Pharmacy “Victor Babeș” Timișoara, have trained family doctors and nurses about the correct BP measurement, investigation of hypertensives, recommendations regarding lifestyle changes, doses and optimal antihypertensive combinations.

**STATISTICAL ANALYSIS**

Data were presented as frequencies and percentages for qualitative variables and as mean ± SD for quantitative variables. Differences between groups of variables were assessed with the Pearson χ² for qualitative variables and the Student t test for quantitative data. The independent variables with a p < 0.05, were considered as having statistical significance. All the statistical analyses were performed using the software Stata 9.2.

**RESULTS**

Of the 5210 hypertensive diagnosed in 19 family offices of Timiș County, a number of 3145 were evaluated during and after a monitoring period of 12 months, having two or more medical visits at their family doctor. After one year of starting treatment a number of 1008 patients (32.05%) had controlled hypertension and office blood pressure (OBP) under the targets of 140/90 mmHg and a number of 2137 (67.95%)
were considered with uncontrolled hypertension, as they did not reach the target OBP of ≤140/90 mmHg.

Of the 2137 uncontrolled patients (67.95%) a number of 790 underwent and had a validated ambulatory blood pressure monitoring (ABPM), of which 520 ABPM with high mean 24h blood pressures, these cases were referred to a hypertension specialist. Of these, a number of 85 (16.35%) were established as untreated, a number of 360 (69.23%) were uncontrolled as they presented uncontrolled BP with therapy, 42 (8.08%) were diagnosed with resistant hypertension and 33 (6.34%) with secondary hypertension.

As concerning the whole 790 number of hypertensive with ABPM, 520 (65.82%) presented uncontrolled hypertension after 12 months of follow up. Their mean age was 53.4±14.4, a family history of premature cardiovascular disease was present in 724 (23.02%), 2140 cases (68.04%) were aware of hypertension, male gender presented 1542 cases (49.03%). Mean duration of hypertension was 14±8.6 years, smoking was present in 663 (21.08%), lipid disorders in 1227 (39.01%), obesity BMI >30 kg/m² in 1353 (43.02%) and visceral obesity 1852 (58.88%), metabolic syndrome was present in 1637 (52.05%), diabetes mellitus in 633 (20.12%), subclinical target organ damage in 818 (26%) and clinical cardiovascular and renal disease in 596 (18.95%).

As concerning the visits to the family doctor, more than 2 visits were present in 3145 patients (100%); 3-4 visits in 1887 (60%), 5-6 visits in 950 (30.2%) and ≥7 visits in 308 (9.8%).

As expected, systolic and diastolic BP values were lower in controlled than uncontrolled patients. Body mass index rose over time in both groups and was higher in uncontrolled patients. Lipid disorders declined over time in both groups, being lower in controlled patients. The prevalence of metabolic syndrome and diabetes mellitus increased over the 5 years of study and was more common in uncontrolled than controlled patients. Clinical manifest cardiovascular disease, chronic kidney disease were more

| TABLE I. Characteristics of the total hypertensive population |
|-----------------|-----------------|
| Characteristics of hypertensives monitored 12 months | Number | Percentage |
| Total monitored hypertensive | 3,145 | 100% |
| Uncontrolled hypertension | 360 | 11.44% |
| Age (years) | 53.4±14.4 | - |
| Family history of premature cardiovascular disease | 724 | 23.02% |
| Awareness of hypertension | 2,140 | 68.04% |
| Male gender | 1,542 | 49.03% |
| Mean duration of hypertension (years) | 14±8.6 | - |
| Smoking | 663 | 21.08% |
| Lipid disorders | 1,227 | 39.01% |
| Obesity BMI >30 kg/m² | 1,353 | 43.02% |
| Visceral obesity | 1,852 | 58.88% |
| Metabolic syndrome | 1,637 | 52.05% |
| Diabetes mellitus | 633 | 20.12% |
| Subclinical target organ damage | 818 | 26% |
| Clinical cardiovascular and renal disease | 596 | 18.95% |

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common in uncontrolled than controlled hypertension. The percentage of hypertensive patients with CKD did not change significantly with time.

The majority of cases with uncontrolled hypertension, 377 (72.5%), presented a high cardiovascular risk, consisting usually of more than 4 risk factors. Intermediate risk was present in 105 (20.2%) and low risk only in 38 (7.3%).

Lifestyle factors associated with uncontrolled hypertension were: obesity in 250 cases (48.07%), physical inactivity in 245 cases (47.11%), high salt intake in 130 (25%), and excessive alcohol intake in 52 patients (10%).

Causes of uncontrolled hypertension were lack of adherence to therapy in 260 cases (50%), inadequate treatment in 208 (40%), blood pressure elevating co-medication in 35 (6.37%), re-

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Uncontrolled HT</th>
<th>Controlled HT</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62±12.4</td>
<td>52±11.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age &gt;60 years</td>
<td>66.34% (345)</td>
<td>54% (297)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Male</td>
<td>51.34% (267)</td>
<td>49.09% (270)</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking</td>
<td>24.03% (125)</td>
<td>17.27% (95)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>40% (208)</td>
<td>36% (198)</td>
<td>NS</td>
</tr>
<tr>
<td>BMI &gt;30 kg/m²</td>
<td>48.07% (250)</td>
<td>34.9% (192)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Visceral obesity</td>
<td>61.15% (318)</td>
<td>42% (231)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>32.11% (167)</td>
<td>18% (99)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Metabolic syndrome</td>
<td>56.15% (292)</td>
<td>44% (242)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Duration of HT (years)</td>
<td>15±8.9</td>
<td>10.1±8.1</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Target organ damage</td>
<td>28.26% (147)</td>
<td>17.09% (94)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>22.11% (115)</td>
<td>16.72% (92)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

**TABLE II. Characteristics of controlled vs. uncontrolled hypertension**

**FIGURE 2. Number of visits/year to the family doctor**

**FIGURE 3. Blood pressure values in controlled and uncontrolled hypertension**

**FIGURE 4. Cardiovascular risk in uncontrolled hypertension**

**FIGURE 5. Lifestyle factors associated with uncontrolled hypertension**
sistant hypertension in 37 (7.11%), secondary hypertension in 32 patients (6.15%) and other causes in 26 cases (5%).

![Figure 6. Causes of uncontrolled hypertension](image)

ABPM and 24-h blood pressure profile in uncontrolled hypertension showed a higher proportion of nondipper pattern (65% vs. 62%) compared with controlled HT.

![Figure 7. ABPM profile in uncontrolled and controlled hypertension](image)

Target organ damage was present in 223 cases (42.88%) of uncontrolled hypertension and in 121 (22%) controlled. Manifest cardiovascular or renal disease was present in 145 (27.88%) of uncontrolled vs. 104 (18.9%) controlled hypertension.

![Figure 8. Cardiovascular/renal disease in uncontrolled and controlled hypertension](image)

The number of BP medications increased over time in both treated uncontrolled and controlled patients. Treatment with no drug was present in 47 cases (9.04%), with 1 drug in 73 cases (14.04%), with 2 drugs in 356 cases (68.46%), with 3 drugs in 33 cases (6.35%) and ≥4 drugs in 11 patients (2.11%).

![Figure 9. Number of drugs used in uncontrolled hypertension](image)

The percentage of uncontrolled patients on 1 medication felt, whereas the percentage on >2 medications rose with time from study start. Therapeutic inertia in uncontrolled hypertension declined over years from study start. In 35% of uncontrolled hypertensive patients we detected a moderate or high level of therapeutic inertia. Angiotensin-converting enzyme inhibitors, beta-blockers, and calcium channel blockers were the agents most often recommended to patients taking a single antihypertensive medication. Our data suggest that medication selection affects control, as patients uncontrolled, compared with controlled on 1 to 2 BP medications, were more rarely taking a diuretic or an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker.

**DISCUSSIONS**

Uncontrolled hypertension is an increasingly common problem in hypertension that needs urgently to be reduced as it may affect as many as 60-75 % of the hypertensive population, becoming an important healthcare problem (3).

Studies of the management of uncontrolled hypertension are few, and strategies are based largely on observational data. In the SEPHAR II Study the rate of control was 25%, being higher, till 39% only in regions with developed socioeconomic level (3,4).

Screening efforts to raise hypertension awareness, especially among medically underserved population groups and individuals at low risk, should include regular use of primary care and plans to engage family doctors and nurses in hypertension care. That will contribute to lower the substantial burden of untreated and uncontrolled hypertension (5).
Uncontrolled hypertensive patients on 1 to 2 BP medications are older and have greater risk for CHD than controlled hypertensive. Interventions to reduce therapeutic inertia are directed to health care providers and patients, as they can improve BP control and reduce cardiovascular risk (6).

As concerning the clinical characteristics of patients whose hypertension is uncontrolled, they have more target-organ damage and a higher long-term cardiovascular risk, than patients whose blood pressure is controlled (7). Heart failure, stroke, myocardial infarction, and renal failure are related to the degree of blood pressure elevation. Other risk factors, such as diabetes and dyslipidemia, further increase the cardiovascular risk in these patients (2).

ABPM is mandatory to exclude the “white-coat” effect. In our database, from 790 treated patients with ABPM, only 520 had 24-hour values ≥140 and/or 90 mmHg, the remaining were considered as having a “white coat” effect. This is also in agreement with previous reports, where the “white-coat” effect was present in 20% to 40% of patients with uncontrolled hypertension monitored in primary care referral units. The uncontrolled hypertension group consisted more frequently of patients with male gender, a longer duration of hypertension, a worse cardiovascular risk profile, a greater proportion of metabolic syndrome, diabetes, smokers, TOD and history of previous CV events (8).

The examination of the circadian BP pattern, showed also differences, as patients with uncontrolled HT presented more frequently an abnormal nocturnal nondipper pattern (low dipper, reverse dipper and extreme dipper), related generally to a worse cardiovascular risk profile (1, 7).

A series of clinical data and studies suggest that the careful evaluation of the patient’s adherence to adequate therapy and lifestyle factors often reveals modifiable contributors to uncontrolled hypertension. Other causes, including administration of exogenous substances (nonsteroidal anti-inflammatory drugs, sympathomimetics as decongestants, anorectics, amphetamines, other illicit drugs, adrenal steroid hormones and oral contraceptive hormones) must also be considered.

A suboptimal medical regimen has been shown to be the primary cause of uncontrolled hypertension in a majority of patients in these studies. An important culprit that contributes to the genesis of uncontrolled hypertension is clinical inertia, defined as the conscious decision of a clinician to treat not adequately a condition, despite knowing that it is present. Clinical inertia may be due to lack of training and experience in the proper use of antihypertensive agents or an overestimation of care already provided. Several studies suggest that this phenomenon is frequent among physicians and represents an important culprit working against the efforts to improve hypertension control rates in the population (2).

Patients should be encouraged to engage to a healthier lifestyle (reduce their intake of sodium, lose weight, have moderate physical exercise and reduce alcohol intake) (2, 9).

The different causes of uncontrolled hypertension are presented in Fig. 11.

![FIGURE 10. Clinical characteristics of uncontrolled hypertension](image)

A poor adherence to treatment may be due to side effects of the medication, sometimes to a large number of tablets which are daily administered. Treatment failure to lower BP, increased costs of drugs, lack of education and information of the patient, the presence of memory or mental disorders and a difficult relationship with the physician contributes also to uncon-
trolled HT (6). In our study, poor adherence to treatment was detected in 50%, but we appreciate that this proportion could be higher, as we did not determined drugs serum concentrations (10).

Studies have shown that 20-40% of hypertensive patients discontinue their treatment within the first year and only less than 40% of the patients will continue the treatment after 5-10 years (2,11). An inverse relationship exists between early treatment discontinuation and the number of doses/day. Factors that improved adherence were selection of agents with reduced side effects (RASB), avoidance of complicated treatment schemes (preferably once daily, fixed combination) and an improved communication doctor patient (5,7). In RESIST-POL study, by serum drug dosing, an increased non-adherence to treatment has been found. Only 13.9% of patients had for all the drugs concentrations above the limit of quantification, 86.1% experienced at least one drug under the limit and 13.9% had no detectable drug (12). Adherence to therapy may be increased by a system of follow-up reminders and telephone calls. The involvement of nurses, who have more time than the family doctors to discuss about the importance of treatment in achieving BP targets, potential side effects of medications, have improved patients’ BP control.

Low compliance is difficult to prove, because patients and their family often do not recognize it. When low compliance is suspected, the family doctor should estimate the daily tablets consumption, administer the medication under observation and recommend dosing of blood concentrations of drugs or urinary metabolites (13).

Because volume overload is common among patients with uncontrolled hypertension, it is important to add or increase diuretic therapy. If the glomerular filtration rate is 30 to 50 ml per minute loop diuretics should be used.

A useful strategy is to combine agents from various classes, each of which has one or more of the following effects: a reduction in volume overload (diuretics and aldosterone receptor antagonists), a reduction in sympathetic overactivity (beta-blockers), a decrease in vascular resistance (through the inhibition of the renin-angiotensin system with the use of ACE inhibitors or angiotensin-receptor blockers) and the promotion of smooth-muscle relaxation (dihydropyridine calcium channel blockers) and alpha-blockers. For example, adding a beta-blocker or ACE inhibitor may counteract the stimulation of the renin-angiotensin system by diuretics or calcium channel blockers (1,10,14).

Some logical combinations include a diuretic with an ACE inhibitor, a beta-blocker, or an angiotensin receptor blocker or an ACE inhibitor with a calcium-channel blocker. In some instances, it may be necessary to increase the dose or the frequency of administration from once to twice daily or to include an additional drug (10).

Referral to a hypertension specialist should be considered in patients whose hypertension is difficult to control, despite assessment of adherence, dose and other factors that may exacerbate the condition.

Integrated healthcare research, policy, and delivery initiatives to the population are needed to reverse growth of unhealthy lifestyles and obesity, to enhance regular use of medication, reduce therapeutic inertia, to develop more ef-
ficacious antihypertensive agents and to improve methods for selecting effective antihypertensive combinations for individual patients.

**CONCLUSIONS**

1. The prevalence of uncontrolled hypertension was 67.95% in our study.
2. ABPM detected in 34.18% of these patients normal mean 24-h values, so these patients were classified with “white-coat” effect.
3. Causes of uncontrolled HT were most frequent medication related (non-adherence, low doses, inadequate combinations), excessive dietary sodium, obesity, secondary and resistant hypertension.
4. Uncontrolled hypertensives, in comparison with controlled ones were more frequently older, smokers, had a longer duration and a more severe hypertension, more often obesity, diabetes mellitus, TOD and cardiovascular disease.

**REFERENCES**