ORIGINAL ARTICLE

Choice of treatment based on Turkish hypertension consensus report: Do we follow the recommendations?

Türk hipertansiyon uzlaşı raporu kılavuzluğunda tedavi seçimi: Önerilere ne kadar uyuyoruz?

Gülden Yürüyen, M.D.,[1] İlkim Deniz Toprak, M.D.,[1] Zeki Toprak, M.D.,[2] Murat Akarsu, M.D.,[1] Pınar Demir, M.D.,[1] Yücel Arman, M.D.,[1] Eylem Özgün Çil, M.D.,[1] Mustafa Özcan, M.D.,[1] Sedat Irmak, M.D.,[1] Özgür Altun, M.D.,[1] Şengül Aydın Yoldemir, M.D.,[1] Hasan Eruzun, M.D.,[1] Tufan Tükek, M.D.[3]

[1]Department of Internal Medicine, İstanbul Okmeydanı Training and Research Hospital, İstanbul, Turkey
[2]Department of Internal Medicine, İstanbul Şişli Hamidiye Etfal Training and Research Hospital, İstanbul, Turkey
[3]Department of Internal Medicine, İstanbul University İstanbul Faculty of Medicine, İstanbul, Turkey

ABSTRACT

Objective: The aim of this study was to determine how often the recommendations of the Turkish Hypertension Consensus Report are followed, and to draw attention to the report.

Methods: The demographic information of 1000 patients diagnosed with hypertension and the details of the antihypertensive medications prescribed at the outpatient service of a tertiary care hospital were recorded, and the data were compared with the recommendations of the report.

Results: The mean age of the patients was 62±11 years. In all, 623 (62.3%) of the 1000 patients were women, and 377 (37.7%) were men. A combination of an angiotensin II receptor blocker (ARB) and a diuretic was the most frequently observed prescription. A diuretic was the most used antihypertensive drug (58.7%), followed by an ARB (48.8%). However, as a monotherapy, a calcium channel blocker (CCB) was the most commonly used antihypertensive drug (19.2%). The most frequently used antihypertensive drug group in older patients was diuretics (63.6%), as proposed in the report. Beta blockers (49.1%) were used more often than expected. For the diabetic group also, a diuretic (60.7%) was the most frequently used antihypertensive drug, followed by an ARB (51.1%) and a CCB (45.2%). Angiotensin-converting enzyme (ACE) inhibitors (34.6%) were the fifth most preferred antihypertensive drug class. However, when ACE inhibitors and ARBs were considered as a single group, known as renin-angiotensin system (RAS) blockers, these RAS blockers were the most prescribed antihypertensive drug class, followed by diuretics. In the group of patients with coronary artery disease, treatment was found to be generally consistent with the report, but the use of diuretics was greater than expected. Lastly, 124 of 160 patients who had chronic kidney disease were given RAS blocker therapy, which was in line with the consensus report recommendations.

Conclusion: Antihypertensive therapies were individualized, as suggested by the consensus report. However, there are proposals still to be considered in special patient groups.

ÖZET

Amaç: Amacımız, 2015 yılında oluşturulmuş olan Türk Hipertansiyon Uzlaşı Raporu önerilerinin, antihipertansif seçiminde ne ölçüde uygulanmış olduğunu ortaya koymak, hekimlerin dikkatlerini uzlaşı raporuna ve tedavi seçimlerine çekmektir.

Yöntemler: Çalışmaya 3. basamak sağlık kuruluşuna hipertansiyon tanısı ile başvuran 1000 hasta alındı. Hastaların son bir yıldır kullanmış olduğu antihipertansif ilaçları, yaşları, cinsiyetleri ve kronik hastalıkları tespit edildi. Uygulamalar uzlaşı raporunun önerileri ile karşılaştırıldı.

Bulgular: Örneklemimizin yaş ortalaması 62±11 olup 623'ü (%62.3) kadın, 377'si (%37.7) erkekti. Anjiyotensin reseptör blokerleri (ARB) + diüretik kombinasyonu en çok tercih edilen reçete şeklini oluşturmaktaydı. En sık kullanılan ilaç grubu birinci sırada %58.7 ile diüretikler, ikinci sırada %48.8 ile ARB'lerdi. Fakat, monoterapide kalsiyum kanal blokerleri (KKB) %19.2 ile en sık kullanılan ilaç grubunu oluşturmaktaydı. Yaşlı hasta grubunda raporda önerildiği gibi çoğunlukla diüretik (%63.6) kullanılmıştı. Ancak beta blokerlerin kullanım oranı %49.1 ile beklenenin üzerinde bulundu. Diyabetik grupta %60.7'lik tercih oranıyla diüretikler birinci sırada yer alırken, ARB'ler %51.1 ile ikinci, KKB'ler %45.2 ile üçüncü sırada yer almaktaydı. Anjiyotensin dönüştürücü enzim (ACE) inhibitörleri ise %34.6 ile beşinci sırada yer alıyordu. Fakat diyabetik hastalar için ACE inhibitörleri ile ARB'leri "renin anjiotensin sistemi (RAS) blokerleri" adı altında topladığımızda, RAS blokerleri tercih sıralamasında en üst sıraya çıkmakta ve diüretikler ikinci sıraya gerilemektedir. Koroner arter hastalığı olan grupta genel olarak rapor ile uyumlu tedaviler verilmiş iken, diüretik kullanımı beklenenin üzerindeydi. Kronik böbrek hastalığı olan 160 hastanın 124'ünde RAS blokeri seçildiği tespit edildi. Bu durumda, kronik böbrek hastalığı olan hastalar için seçilen tedaviler, raporla uyumlu görünmektedir.

Sonuç: Raporun önerdiği şekilde hasta bazında kişiselleştirilmiş tedavi uygulamalarının varlığına rağmen, hala özel hasta gruplarında dikkat edilmesi gereken öneriler bulunmaktadır.

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Correspondence: Dr. İlkim Deniz Toprak. Okmeydanı Eğitim ve Araştırma Hastanesi, İç Hastalıkları Kliniği, 34384 Şişli, İstanbul, Turkey.
Tel: +90 212 - 314 55 55 e-mail: ilkimdenizzz@hotmail.com

Hypertension is the most important modifiable risk factor for myocardial infarction, stroke, congestive heart failure, end-stage renal disease, and peripheral vascular disease.[1] The prevalence, awareness, treatment, and control of hypertension in Turkey (PatenT) study, which examined the distribution of blood pressure (BP) and hypertension in Turkey in 2003, demonstrated that the prevalence of hypertension was very high (31.8%).[2] In 2010, the Hypertension incidence in Turkey (HinT) study, the first to investigate the incidence of hypertension in Turkey, determined the rate to be 21.3%. This rate is relatively high for a young population such as that of Turkey.[3]

Abbreviations:

ACE	*Angiotensin-converting enzyme*
ARB	*Angiotensin receptor blocker*
BP	*Blood pressure*
CCB	*Calcium channel blocker*
RAS	*Renin angiotensin system*

Hypertension causes a substantial national burden due to its complications. In 2015, the Turkish Hypertension Consensus Report was published by specialist academics of the Turkish Society of Cardiology, the Turkish Society of Internal Medicine, the Turkish Society of Endocrinology and Metabolism, the Turkish Society of Nephrology, and the Turkish Society of Hypertension and Kidney Diseases.[4] In the diagnosis and treatment of hypertension, Turkish physicians often use the European or American guidelines. However, there are differences in the guidelines, and some of the recommendations are not consistent with clinical practice in our country. The lucidity and easy clinical applicability of the Turkish Hypertension Consensus Report has drawn the interest of physicians.

The primary goal of this study was to determine which antihypertensive treatment modalities were used before the report was published, particularly in special patient groups, and thus to identify the medication choices of physicians and their cohesion with the report. The secondary aim was to draw attention to the Turkish Hypertension Consensus Report and to increase physicians' awareness to promote treatment that is more consistent with the consensus report.

METHODS

The study was designed as a retrospective, observational, cross-sectional, analytic study. A total of 1000 randomly selected patients who presented with hypertension to the tertiary care outpatient services of internal medicine, nephrology, cardiology, and endocrinology were enrolled. Essential hypertension patients aged over 30 years were included in the study after approval was granted by the local Ethics Committee. Patients with secondary hypertension and those who were pregnant or aged less than 30 years were excluded.

Comorbid diseases and antihypertensive medications used by the patients in the prior year were recorded according to hospital information system demographic information (age and sex).

As stated in the report, after reviewing the patients' past medical records using up-to-date guidelines, the patients were categorized into 4 groups: patients older than 65 years, patients with diabetes mellitus, those with chronic renal failure, and patients with coronary artery disease. The diagnosis of diabetes was made by specialists according to the Guide to Diagnosis, Treatment, and Follow-up of Diabetes Mellitus published by the Turkish Society of Endocrinology and Metabolism. The antihypertensive drugs prescribed were categorized into 5 main groups in line with the Guide to Treatment and Follow-up of Hypertension published by the Turkish Society of Cardiology and the Turkish Hypertension Consensus Report. These groups, according to their historical development, were diuretics, beta blockers, calcium channel blockers (CCB), angiotensin-converting enzyme (ACE) inhibitors, and angiotensin receptor blockers (ARB). Furosemide, which is used for cardiac failure, was excluded from the study. Diuretics included thiazides, spironolactone, and indapamide. Other drugs, such as alpha-blockers or methyldopa were grouped as other medications.

The antihypertensive drugs used by each group were categorized according to the mean value determined with IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY, USA) software and the frequency rate was calculated. The first, second, third, and fourth most prescribed drug groups were identified for each patient group. The data were compared with the recommendations of the Turkish Hypertension Consensus Report.

RESULTS

The mean age of the patients was 62±11 years. In the group, 623 (62.3%) were women and 377 (37.7%)

Table 1. Demographic details and comorbid diseases of 1000 patients

Variables	Frequency % (n=1000)
Age (years)	
<65	540 (54%)
≥65	460 (46%)
Sex	
Female	623 (62.3%)
Male	377 (33.7%)
Comorbidity	
Existing	631 (63.1%)
Not existing	369 (36.9%)
Comorbid diseases	
Diabetes mellitus	418 (41.8%)
Coronary artery disease	275 (27.5%)
Chronic kidney disease	160 (16%)

were men, and 460 (46%) were aged over 65 years. Demographic details and comorbid diseases are provided in Table 1.

The antihypertensive drug prescriptions of the whole study group are illustrated in Figure 1. Diuretics were the most frequently used antihypertensive drug (58.7%), followed by ARBs (48.8%). Among diuretics, the most preferred was a thiazide, with a rate of 87.6%, and was most commonly prescribed as tablets combined with renin angiotensin receptor blockers. Among all diuretics, indapamide, which is prescribed in single tablet form, was selected at a rate of 12.4%. Combination therapy was prescribed for 80.8% of the patients, which demonstrates that it was preferred to monotherapy. The combination of an ARB and a diuretic was the most common prescription.

In all, 37.4% of the 808 patients who used a combination therapy were on dual therapy, and 32% were on triple therapy. The most common combination was an ARB and a diuretic, followed by an ACE inhibitor and a diuretic. Triple therapy prescriptions were mostly combinations of an ARB, a diuretic, and a beta blocker or a CCB. There was no statistically significant difference between the choice of a CCB or a beta blocker. As a third drug, the percentage of the addition of a beta blocker was 8.6%, and it was 8.4% for a CCB ($p>0.05$). A summary of the combination therapies prescribed is shown in Tables 2 and 3.

The antihypertensive drugs selected for specific patient groups were evaluated separately and can be seen in Table 4. Four special patient groups were assessed, as in the consensus report, and other comorbid conditions were excluded.

The consensus report recommends that an ACE inhibitor or an ARB should be the first-line treatment for hypertension when diabetes mellitus is present, and when metabolic syndrome is present, diuretics are relatively contraindicated. In this study, it was determined that a diuretic was the most preferred, with a rate of 60.7%, an ARB was the second choice, with 51.1%, followed by a CCB at 45.2% in patients with diabetes. An ACE inhibitor, which should be the first-line treatment, was the fifth most-chosen medication at 34.6%. Although it is not clear how many patients of our randomly and retrospectively selected patient group had metabolic syndrome, given the fact that the presence of metabolic syndrome is higher in patients with diabetes, the preferences were not consistent with the recommendations of the consensus report since the most prescribed was a diuretic and an ACE inhibitor was fifth. However, when we grouped ACE inhibitors and ARBs together as renin angiotensin system (RAS) blockers, it was determined that 357 of 418 patients with diabetes were receiving RAS blockade therapy and 61 were not. In this case, RAS blockers were the most prescribed antihypertensive drug class, followed by diuretics (254 patients), CCBs (189 patients), and beta blockers (164 patients). When combination therapies and monotherapies were jointly

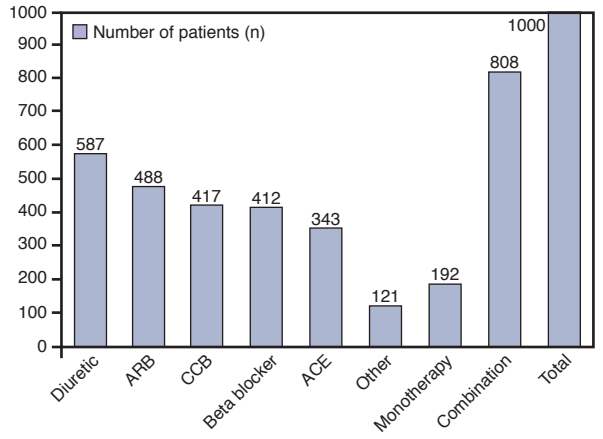

Figure 1. Antihypertensive drug preferences.

ACE: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin receptor blocker; CCB: Calcium-channel blocker.

Table 2. Combination therapies

Antihypertensive drugs	The total number of patients		First preference
	n	%	
Dual therapy	374	37.4	ARB + Diuretic
Triple therapy	320	32	ARB + Diuretic + Beta Blocker / CCB
Quadruple therapy or more	114	11.4	ARB + Diuretic + Beta Blocker + CCB

ARB: Angiotensin receptor blocker; CCBs: Calcium-channel blocker.

Table 3. Ranked preferences in combination therapy

Preference number	Dual therapy	Triple therapy
1	Angiotensin receptor blocker + Diuretic	Angiotensin receptor blocker + Diuretic + Beta blocker
2	ACE + Diuretic	Angiotensin receptor blocker + Diuretics + CCB
3	ACE + CCB	ACE + Diuretic + Beta blocker
4	Angiotensin receptor blocker + CCB	ACE + Diuretic + CCB

ACE: Angiotensin-converting enzyme inhibitor; CCB: Calcium-channel blocker.

Table 4. Antihypertensive drugs selected for specific patient groups

Patient groups / drug choice	First preference (%)	Second preference (%)	Third preference (%)	Fourth preference (%)
Elderly (≥65 year-old)	Diuretic (63.6)	Beta blocker (49.1)	ARB (48.2)	CCB (47.8)
Diabetes mellitus	Diuretic (60.7)	ARB (51.1)	CCB (45.2)	Beta blocker (39.2)
Coronary artery disease	Beta blocker (71.9)	Diuretic (56.1)	CCB (44.5)	ACE (41.4)
Chronic kidney disease	Diuretic (59.3)	Beta blocker (58.7)	CCB (50.6)	ARB (47.5)

ACE: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin receptor blocker; CCB: Calcium-channel blocker.

evaluated, it was observed that the combination of a RAS blocker and a diuretic was the most preferred (21%) prescription.

In the consensus report, diuretics and CCBs are recommended for the elderly. The data revealed that the first choice (63.6%) in prescriptions for these patients was a diuretic, as suggested in the consensus report. However, the use of a CCB was the fourth choice (47.8%). The consensus report does not recommend beta blockers as a first-line therapy for older patients without a specific indication. In the present study, beta blockers were the second most prescribed antihypertensive drug in almost half of the older patients (49.1%). In the elderly group, beta blocker use was greater than expected when one considers that the rate of coronary artery disease was 37%.

The consensus report recommends that beta blockers, ACE inhibitors, CCBs, or ARBs can be used for patients with coronary artery disease, with no specification regarding the order of preference. In the current study, the most commonly selected were beta blockers, diuretics, CCBs, and ACE inhibitors, respectively, and in this group too, the use of diuretics was greater than expected. A thiazide was the most frequently prescribed diuretic.

It is recommended in the consensus report that antihypertensive therapy should begin with an ACE inhibitor or an ARB if chronic kidney disease is present. In our study, a diuretic was the most preferred antihypertensive drug class for patients with chronic kidney disease, followed by a beta blocker. An ARB was the fourth most often selected medication, and an ACE inhibitor was fifth. According to the consensus report, the treatment for patients with chronic kidney disease

Table 5. Therapies according to comorbidities

Diseases	Age ≥65 years	First preference drug	First preference combination
Only HT (n=369)	140 (37.9%)	Diuretic	ARB + Diuretic
HT + DM (n=268)	95 (35.4%)	Diuretic	ARB + Diuretic
HT + CAD (n=136)	74 (54.4%)	B-blocker	ACE + Diuretic + B-blocker
HT + DM + CAD (n=67)	41 (61.1%)	B-blocker	RAS + Diuretic + B-blocker / CCB
HT + DM + CAD + CKD (n=52)	32 (61.5%)	B-blocker	RAS + Diuretic +B-blocker / CCB
HT + CKD (n=47)	33 (70.2%)	Diuretic	ARB + Diuretic + B-blocker
HT + DM + CKD (n=31)	21 (67.7%)	Diuretic	ARB + Diuretic + B-blocker / CCB
HT + CAD + CKD (n=30)	24 (80%)	B-blocker	ACE + Diuretic + B-blocker + A-blocker

A-blocker: Alpha-blocker; ACE: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin receptor blocker; B-blocker: Beta blocker; CAD: Coronary artery disease; CCB: Calcium-channel blocker; CKD: Chronic kidney disease; DM: Diabetes mellitus; HT: Hypertension; n: number of patients; RAS: Renin angiotensin aldosterone system blocker. The combinations of diseases are arranged in descending order based on the number of patients, from top to bottom.

should be individualized, considering the age of the patient, comorbidities (diabetes mellitus, cardiovascular disease), and if the patient is undergoing dialysis treatment. Given that the treatment recommended for patients with chronic kidney disease in this study was individualized, the choice of antihypertensive therapy seems to be consistent with the report. Nevertheless, the choice of a diuretic as the most preferred medication was greater than expected. Again, the overuse of beta blockers was not consistent with the recommendations of the consensus report. However, when ACE inhibitors and ARBs were grouped together as RAS blockers for patients with chronic kidney disease, it was determined that CCBs were the most often selected antihypertensive medication as a monotherapy, followed by beta-blockers, RAS blockers, and others, respectively. When the combination therapies and monotherapies were jointly evaluated, it was seen that combinations of a RAS blocker, a diuretic, and a beta blocker (16.8%) were the most preferred prescriptions. Of 160 patients, 124 who had chronic kidney disease were receiving RAS blockade therapy. Therefore, the selected treatments were more compatible with the consensus report.

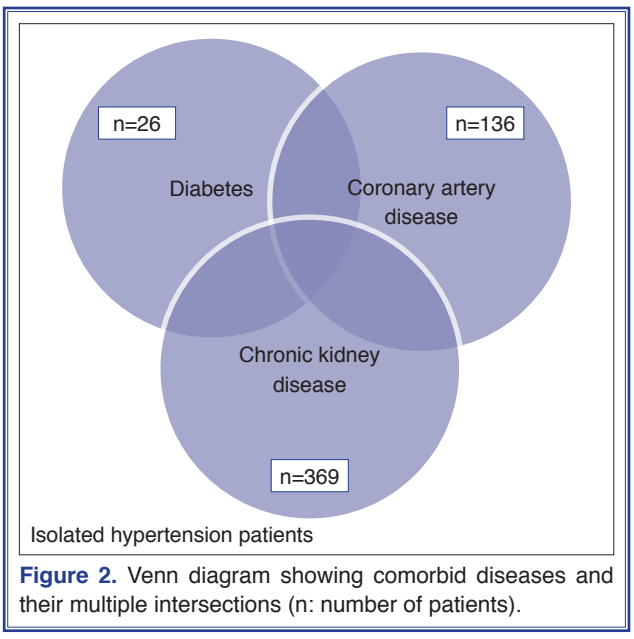

Figure 2. Venn diagram showing comorbid diseases and their multiple intersections (n: number of patients).

The present study was conducted with patients of a tertiary care outpatient service. Admissions to the hospital consist of complicated cases and patients usually have more than one comorbid disease. Given these conditions, physicians generally prefer to prescribe individualized antihypertensive medications. Multiple intersection sets can be seen in the Venn diagram illustrating comorbidities in Figure 2.

Of 1000 patients, 36.9% had no comorbidities; they were using antihypertensive medication to treat hypertension only. This group also had the youngest mean age. In this group, a thiazide diuretic used in combination therapy was the most frequently used antihypertensive drug, followed by an ARB. The most common combination (also more than monotherapy) was an ARB and a diuretic, and this preference was consistent with the recommendations of the consensus report.

The therapies of the patients according to comorbidities are provided in Table 5. The first 2 groups of patients, those with hypertension alone and hypertension with diabetes mellitus, accounted for more than

half (63%) of the total number. In the rest of the sample, patients aged over 65 years were in the majority. Moreover, the preference for a beta blocker was greater in this remainder of the sample. It is known that the incidence of coronary artery disease is significantly greater in this same group; therefore, beta blockers are not considered to be the wrong choice.

Another finding of this study was that as the number of comorbid conditions increased, so did the drug diversity and more drugs were used in combination therapies. The individualized therapy preferences used vis-à-vis comorbidities were compatible with the consensus report.

DISCUSSION

If the current literature is reviewed, it can be seen that there are many studies about the incidence, prevalence, diagnosis, treatment, complications, cost, and awareness of hypertension. The literature provides information about how successfully different antihypertensive therapies have controlled blood pressure. However, a comprehensive study about what kind of antihypertensive therapy is preferred and whether the preferences were in agreement with current guidelines was not found. The present study could lead physicians to prescribe more effective treatments and better control hypertension, which is important since hypertension is a major public health problem in terms of complications and burden of disease.

Our study was conducted after the publication of the Turkish Hypertension Consensus Report in the Archives of Turkish Society of Cardiology; however, the therapies preferred by physicians in the previous year were identified retrospectively. Therefore, these treatments were all initiated before the consensus report was published. The consensus report, as a common synthesis of domestic and foreign current hypertension guidelines, is important as a practical first reference source for Turkish physicians. A cross-sectional and observational original study, such as ours, was needed to draw attention to this subject.

In Turkey, there is no other original study reporting antihypertensive drug consumption and prescription patterns, but similar studies can be found in the international literature. In August 2016, Bakare et al.[5] identified antihypertensive treatment prescription patterns and frequently preferred drug classes in a training hospital in Nigeria. Patients in that study were most often prescribed combination therapy, and diuretics were the most frequently used antihypertensive drug (64%), as it was in the present study. Triple combination therapy was most preferred in the study conducted by Bakare et al. In contrast, in our study, dual-combination treatments were most prescribed. ARBs were the fifth antihypertensive drug group of choice in their study (16.5%). This may be due to the higher cost of ARBs, which are the newest antihypertensive drugs. Correspondingly, in the same study, it was indicated that antihypertensive prescription costs constituted a barrier to effective antihypertensive treatment. In our study, almost half (48%) of the patients were using an ARB. Our results indicated that there was no problem in terms of access or use of ARBs. When the Turkish Hypertension Consensus Report suggests RAS blockers, it does not distinguish one from another (ACE inhibitor or ARB). Physicians have a tendency to prescribe an ARB, even though ACE inhibitors are more affordable. This should perhaps be explored in another study.

In research conducted in Bosnia and Herzegovina, Selmanovic et al.[6] reported that ACE inhibitors were the most frequently prescribed antihypertensive drug (20.2%), followed by the combination of an ACE inhibitor and a CCB. In the retrospective cohort study of Schulz et al.[7] performed in Germany, beta blockers (42.5%) and ACE inhibitors (31.9%) were identified as the most commonly prescribed antihypertensive drug groups. In our study, the most commonly used combination was an ARB and a diuretic, which indicates that antihypertensive prescribing tendencies may be different between countries.

In the elderly, contrary to guideline recommendations, beta blockers were found to be overused, and CCBs were used less. In patients with diabetes, despite the frequent use of a RAS blocker, the use of a diuretic was high and the use of a CCB was low. There was a tendency to avoid RAS blockers in patients with chronic kidney disease. It is interesting that the use of beta blockers in these patients was excessive. Both the overuse of diuretics and the underuse of CCBs indicate a problem at this point. Given that these data predate the consensus report, it would not be wrong to say that the report will meet an important need. In the future, further studies are required to assess its impact.

Conclusion

Our study revealed that dual combination therapy was the most frequently preferred therapy for hypertension. The most commonly used antihypertensive drugs were diuretics and ARBs. The use of an individualized therapy due to comorbidities was consistent with the consensus report. The study results also indicate that the Turkish Hypertension Consensus Report is widely used in clinical practice.[4] However, there are still issues that need to be considered, especially in special patient groups.

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