ONKOHIPERTENZIJA – NOVI KLINIČKI ENTITET U SAVREMENOJ MEDICINI

STRUČNI ČLANCI

PROFESSIONAL ARTICLES

ONCO-HYPERTENSION – A NEW CLINICAL ENTITY IN MODERN MEDICINE

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SAŽETAK

Kardiovaskularna i onkološka oboljenja u savremenom dobu predstavljaju neizostavni deo svakodnevne medicinske prakse na svim nivoima zdravstvene zaštite. Osim zajedničkih faktora rizika, ova oboljenja povezana su i na druge načine, a posebno je značajna potencijalna kardiotoksičnost antineoplastičnih lekova. Jedan od čestih oblika kardiotoksičnosti antineoplastične terapije je hipertenzija. S obzirom na to da se može manifestovati bilo kada tokom primene antineoplastične terapije, ali i po završetku specifičnog onkološkog lečenja, onkohipertenzija je klinički entitet o kojem uvek treba razmišljati pri susretu sa onkološkim pacijentima. Redovna kontrola arterijskog krvnog pritiska u ovoj populaciji neophodna je kako bi se obezbedilo blagovremeno prepoznavanje i lečenje onkohipertenzije, u cilju bezbednog sprovođenja onkološkog tretmana. Iako smernice za lečenje onkohipertenzije ne odstupaju značajno od opštih preporuka za lečenje hipertenzije, postoje određene specifičnosti koje se najpre odnose na izbor antihipertenziva i odstupanja u smislu ciljnih vrednosti arterijskog krvnog pritiska, u zavisnosti od stadijuma onkološkog oboljenja i prognoze. Veoma je važno prepoznati i momenat kada je neophodno obustaviti kardiotoksičnu antineoplastičnu terapiju ili redukovati dozu antineoplastičnog leka, kako bi se izbegle životno ugrožavajuće kardiovaskularne posledice. Složenosti problema onkohipertenzije značajno doprinose i brojni faktori koji se susreću kod onkoloških pacijenata, poput komorbiditeta, prisustva bola ili drugih primenjenih lekova. S obzirom na to da se radi o veoma osetljivoj populaciji izloženoj posebnoj vrsti psihološkog stresa, posebno treba imati u vidu i mogućnost „efekta belog mantila", kao i maskiranu hipertenziju.

Ključne reči: hipertenzija, maligna oboljenja, kardiotoksičnost

ABSTRACT

Cardiovascular and oncological diseases represent an inevitable part of everyday medical practice at all levels of health care. Apart from common risk factors, these diseases are associated in other ways, and the potential cardiotoxicity of antineoplastic drugs is particularly significant. One of the frequent forms of cardiotoxicity is hypertension. Considering that it can manifest at any time during antineoplastic therapy and also after the completion of specific oncological treatment, onco-hypertension is a clinical entity that should always be kept in mind when caring for oncology patients. Regular arterial blood pressure checks in this population are necessary to ensure timely recognition and treatment of onco-hypertension and to carry out oncological treatment safely. Although the guidelines for the treatment of onco-hypertension are similar to the general recommendations for hypertension, some specificities primarily concern the choice of antihypertensive drugs and exceptions to target arterial blood pressure values depending on the stage of the oncological disease and its prognosis. It is crucial to recognize the time to stop cardiotoxic antineoplastic therapy or reduce the dose of the antineoplastic drug to avoid life-threatening cardiovascular complications. Numerous additional factors encountered in oncology patients, such as comorbidities, the presence of pain or other administered drugs, significantly contribute to the complexity of onco-hypertension. Given that this is a very sensitive population exposed to a specific type of psychological stress, the possibility of the "white coat effect" as well as masked hypertension should also be considered.

Keywords: hypertension, malignant diseases, cardiotoxicity

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UVOD

Pojam kardiotoksičnosti u sklopu lečenja onkoloških oboljenja pomenut je još početkom 70-ih godina prošlog veka [1]. Tokom 2020. godine širom sveta je dijagnostikovano skoro 20 miliona novih slučajeva malignih oboljenja, a iste godine je oko 10 miliona onkoloških pacijenata preminulo [2]. U proteklih 30 godina broj pacijenata sa hipertenzijom se udvostručio, tako da ih je 2019. godine bilo 1,3 milijardi u celom svetu [3]. Od približno 20 miliona kardiovaskularnih smrtnih ishoda godišnje, oko 50% slučajeva povezuje se upravo sa hipertenzijom [4,5]. Zbog svega gore navedenog, 2022. godine objavljen je prvi evropski vodič posvećen oblasti kardioonkologije [6]. Ipak, od svih kardiovaskularnih oboljenja, hipertenzija je najčešći komorbiditet onkoloških pacijenata [7]. Učestalost hipertenzije u populaciji onkoloških bolesnika je oko 40%, što je značajno više nego u opštoj populaciji. Shodno tome, u literaturi se tokom proteklih nekoliko godina pojavio novi pojam, onkohipertenzija [8].

Cilj rada je sagledavanje povezanosti hipertenzije, onkoloških oboljenja i antineoplastične terapije. Dodatni cilj je isticanje preporuka za lečenje onkohipertenzije i specifičnosti ovog terapijskog pristupa koje je potrebno imati u vidu na svim nivoima zdravstvene zaštite kako bi se obezbedilo blagovremeno i adekvatno zbrinjavanje pacijenata.

Hipertenzija i maligna bolest

Onkohipertenzija ima četiri osnovna aspekta. Hipertenzija može biti uzrok malignog oboljenja [9–15], ali i posledica malignog oboljenja [16–18] ili primenjene antineoplastične terapije [19]. Ponekad se maligno oboljenje može dovesti u vezu i sa prethodnom antihipertenzivnom terapijom [20,21]. Poznato je da pacijenti sa hipertenzijom imaju oko dva puta veći rizik za nastajanje karcinoma bubrega, posebno ukoliko su vrednosti arterijskog krvnog pritiska preko 160/100 mmHg [9]. Kod muškaraca je ustanovljena povezanost hipertenzije sa kolorektalnim karcinomom i karcinomom prostate [13,14], dok kod žena postoji povezanost hipertenzije sa pojavom karcinoma dojke u postmenopauzalnom periodu [15]. Antihipertenzivna terapija kao uzrok malignih oboljenja je polje koje zahteva dodatna istraživanja. Iz etičkih razloga, nijedna randomizovana klinička studija nije dizajnirana da pruži odgovor na ovo pitanje. Za sada je dodatna pažnja usmerena na diuretike – zbog eventualnog rizika od razvoja karcinoma bubrega, tiazidne diuretike – zbog povećanja rizika za nastajanje skvamocelularnog karcinoma kože, kao i na inhibitore angiotenzin-konvertujućeg enzima – zbog izvesnog povećanja rizika od karcinoma pluća [20–22]. Hipertenzija može biti i po-

INTRODUCTION

The concept of cardiotoxicity in the context of cancer treatment was first mentioned in the early 1970s [1]. In 2020, nearly 20 million new cancer cases were diagnosed worldwide, while approximately 10 million oncology patients died during the same year [2]. Over the past 30 years, the number of patients with hypertension has doubled, reaching 1.3 billion globally in 2019 [3]. Of the approximately 20 million annual cardiovascular deaths, around 50% are directly associated with hypertension [4,5]. Given the facts mentioned above, the first European guideline dedicated to cardio-oncology was published in 2022 [6]. Nevertheless, among all cardiovascular diseases, hypertension remains the most common comorbidity in oncology patients [7]. The prevalence of hypertension among oncology patients is about 40%, which is significantly higher than in the general population. Consequently, in recent years, the term onco-hypertension has emerged in the literature [8].

This paper examines the relationship among hypertension, malignancy, and antineoplastic therapy. An additional goal is to highlight the recommendations for the management of onco-hypertension and the specific therapeutic considerations that must be taken into account at all levels of healthcare to ensure timely and adequate patient management.

Hypertension and Malignancy

Onco-hypertension has four main aspects. Hypertension may be the cause of malignant disease [9–15], a consequence of malignancy [16–18], or the result of antineoplastic therapy [19]. Sometimes malignancy can also be linked to prior antihypertensive treatment [20,21]. It is known that patients with hypertension have approximately twice the risk of developing renal cancer, especially when blood pressure values exceed 160/100 mmHg [9]. Among men, hypertension has been associated with colorectal and prostate cancer [13,14], while in women it has been linked to postmenopausal breast cancer [15]. Antihypertensive therapy as a potential cause of malignancy is an area that requires further investigation. For ethical reasons, no randomized clinical trial has been designed to address this question. Currently, attention is focused on diuretics–due to a possible risk of renal cancer; thiazide diuretics–because of the increased risk of cutaneous squamous cell carcinoma; and angiotensin-converting enzyme inhibitors–due to a potential increase in lung cancer risk [20–22]. Hypertension may also occur as a consequence of malignancy itself, representing a component of paraneoplastic syndromes, such as those associated with renal cell

sledica maligne bolesti, odnosno deo paraneoplastičnog sindroma, što je slučaj kod karcinoma bubrega, hepatocelularnog karcinoma, mekotkivnog sarkoma i karcinoidnog sindroma [16–18]. Ipak, najveću oblast onkohipertenzije predstavlja hipertenzija kao posledica kardiotoksičnosti antineoplastične terapije [19,23]

carcinoma, hepatocellular carcinoma, soft-tissue sarcoma, and carcinoid syndrome [16–18]. However, the most prominent aspect of onco-hypertension is hypertension as a manifestation of cardiotoxicity induced by antineoplastic therapy [19,23] (Table 1). According to literature data, 99% of children treated for

Tabela 1. Grupe antineoplastičnih lekova koji mogu prouzrokovati hipertenziju

ANTINEOPLASTIČNA TERAPIJA	PRIMENA U ONKOLOGIJI	UČESTALOST ONKOHIPERTENZIJE
Inhibitori signalnog puta vaskularnog endotelnog faktora rasta (VEGF-Spi)	Metastatski tumori (renalni, hepatocelularni, tiroidni, gastrointestinalni, stromalni)	20%–90% *U zavisnosti od jačine i doze leka
Derivati platine	Karcinom testisa (najčešći malignitet kod mladih muškaraca), tumori ovarijuma, kolona, mokraćne bešike, pluća i pleure	50%
Inhibitori proteazoma	Multipli mijelom	10%–32% *Ređe kod novijih generacija lekova
Inhibitori Bruton tirozin kinaze (BTK)	Hronična limfocitna leukemija i „mantle cell" limfom	70%
PARP inhibitori (niraparib)	Tumori ovarijuma i dojke	20%
(B)RAF/MEK inhibitori	Melanom i kolorektalni karcinom sa BRAF mutacijom	15%–20%
Inhibitori RET kinaze	Nesitnoćelijski karcinom pluća, tiroidni karcinom	20%–40%
Alkilirajući agensi	Veliki broj solidnih i hematoloških maligniteta	36%, a kod dece 15%–58%
mTOR inhibitori	Renalni karcinom, karcinom dojke i pankreasni neuroendokrini tumori	13%
Inhibitori kalcineurina	Nakon transplantacije matičnih ćelija hematopoeze	30%–60%
Androgen deprivaciona terapija	Karcinom prostate (40% pacijenata)	5%–25%
Inhibitori aromataze	Karcinom dojke (65%–70% pacijentkinja)	8%–13% *Još uvek tema polemike

Table 1. The groups of antineoplastic drugs that may cause hypertension

ANTINEOPLASTIC TREATMENT	TARGET CANCERS	ONCO-HYPERTENSION FREQUENCY
Vascular endothelial growth factor signaling pathway inhibitors (VEGF-Spi)	Metastatic cancers (renal, hepatocellular, thyroid, gastrointestinal, stromal)	20%–90% *Depending on the drug strength and dose
Platinum derivatives	Testicular cancer (the most frequent cancer in young males), ovarian, colorectal, bladder, lung, and pleural cancer	50%
Proteasome inhibitors	Multiple myeloma	10%–32% *Less often with newer generation drugs
Bruton tyrosine kinase (BTK) inhibitors	Chronic lymphocytic leukemia and "mantle cell" lymphoma	70%
PARP inhibitors (nirparib)	Ovarian and breast cancer	20%
(B)RAF/MEK inhibitors	Melanoma and colorectal cancer with BRAF mutation	15%–20%
RET kinase inhibitors	Non-small cell lung and thyroid cancer	20%–40%
Alkylating agents	A large number of solid and hematological cancers	36%, but 15%–58% in children
mTOR inhibitors	Renal, breast and pancreatic neuroendocrine cancer	13%
Calcineurin inhibitors	After stem cell transplantation	30%–60%
Androgen deprivation therapy	Prostate cancer (40% of patients)	5%–25%
Aromatase inhibitors	Breast cancer (65%–70% of patients)	8%–13% *Still a controversial issue

(Tabela 1). Prema literaturnim podacima, 99% dece lečene zbog malignog oboljenja tokom života će razviti neko od hroničnih oboljenja usled prethodno primenjene antineoplastične terapije [19]. Takođe, ustanovljeno je da osobe iz ove populacije do 50. godine života ispolje prosečno oko 17 neželjenih efekata antineoplastične terapije primenjene u detinjstvu, od kojih su 3–5 neželjenih efekata veoma ozbiljni, a potencijalno i životno ugrožavajući [19]. Učestalost hipertenzije kao posledice primene antineoplastične terapije u detinjstvu iznosi 70% do 50. godine života [19].

Onkohipertenzija kao posledica kardiotoksičnosti antineoplastične terapije

Onkohipertenzija kao posledica kardiotoksičnosti antineoplastične terapije javlja se sa učestalošću većom od 10% za većinu klasa antineoplastičnih lekova, što je svrstava u veoma često neželjeno dejstvo [24]. Mehanizmi onkohipertenzije usled kardiotoksičnosti antineoplastične terapije su brojni, različiti i za sada samo delimično poznati. U najčešće mehanizme onkohipertenzije ubrajaju se inhibicija angiogeneze, redukcija kapilarne mreže, poremećaj ravnoteže vazoaktivnih činilaca (najpre snižavanje nivoa azotnog oksida i povećanje nivoa endotelina-1), oksidativni stres, nefrotoksičnost, kao i poremećaji na nivou autonomnog nervnog sistema [24].

Vreme ispoljavanja onkohipertenzije kao kardiotoksičnosti može biti različito [6]. Kod većine antineoplastičnih lekova, hipertenzija može nastati bilo kada tokom primene terapije. Zbog toga se preporučuje merenje krvnog pritiska na svakoj kontroli. Takođe, preporučuje se i merenje krvnog pritiska u kućnim uslovima jednom nedeljno tokom prva tri meseca terapije, a potom jednom mesečno tokom celokupnog trajanja terapije. Ovo je posebno značajno kod hematoloških pacijenata koji su na terapiji inhibitorima Bruton tirozin kinaze jer pacijenti godinama ostaju na ovoj terapiji. Ipak, hipertenzija kao posledica kardiotoksičnosti antineoplastične terapije može nastati i akutno, nakon nekoliko dana od početka primene terapije, što je tipično za inhibitore signalnog puta vaskularnog endotelnog faktora rasta (VEGF-Spi). Kod primene ovih lekova preporučuje se svakodnevno merenje krvnog pritiska tokom prvog ciklusa terapije i pri svakom povećanju doze, a potom na 2–3 nedelje. Iako ima akutni početak, onkohipertenzija prouzrokovana lekovima iz grupe VEGF-Spi je reverzibilna. Takođe, hipertenzija kao posledica kardiotoksičnosti antineoplastične terapije može nastati i odloženo, nakon nekoliko godina od početka terapije, što je karakteristično za derivate platine. Platina se inkorporira u DNK, a cisplatin se u krvi može detektovati i 13 godina nakon primene. Zato

malignant diseases develop at least one chronic condition during their lifetime due to prior antineoplastic therapy [19]. Moreover, individuals from this population experience, on average, 17 adverse effects of childhood antineoplastic treatment by the age of 50, of which 3–5 are severe or potentially life-threatening [19]. The prevalence of hypertension secondary to childhood antineoplastic therapy is as high as 70% by the age of 50 [19].

Onco-hypertension as a Consequence of Antineoplastic Therapy Cardiotoxicity

Onco-hypertension resulting from cardiotoxicity of antineoplastic therapy occurs with a frequency greater than 10% for most classes of antineoplastic drugs, categorizing it as a frequent adverse effect [24]. The mechanisms of onco-hypertension associated with antineoplastic cardiotoxicity are numerous, diverse, and only partially known. The most common mechanisms include inhibition of angiogenesis, reduction of capillary density, imbalance of vasoactive mediators (primarily decreased nitric oxide and increased endothelin-1 levels), oxidative stress, nephrotoxicity, and disturbances of the autonomic nervous system [24].

The timing of onco-hypertension as cardiotoxicity onset varies [6]. For most antineoplastic drugs, hypertension can develop at any time during therapy. Therefore, blood pressure should be measured at each clinical visit. In addition, home blood pressure monitoring is advised once weekly during the first three months of therapy, and monthly thereafter throughout treatment. This is particularly relevant for hematologic patients receiving Bruton tyrosine kinase inhibitors, as these therapies are often continued for years. However, hypertension as a consequence of antineoplastic treatment cardiotoxicity may also develop acutely, within days of treatment initiation, as is typical with vascular endothelial growth factor signaling pathway inhibitors (VEGF-SPi). For these agents, daily blood pressure monitoring is recommended during the first treatment cycle and after each dose escalation, and every 2–3 weeks thereafter. Although it has an acute onset, VEGF-SPi-induced hypertension is reversible. Also, hypertension as a consequence of cardiotoxicity of antineoplastic therapy can occur delayed, years after the initiation of treatment, as seen with platinum-based agents. Platinum becomes incorporated into DNA, and cisplatin can be detected in the bloodstream up to 13 years after exposure. Therefore, these patients require long-term follow-up and sustained blood pressure control [6].

je kod ovih pacijenata potrebno dugoročno praćenje i dugotrajna kontrola arterijskog krvnog pritiska [6].

Ciljne vrednosti arterijskog krvnog pritiska kod lečenja onkohipertenzije

Kod pacijenata sa malignim oboljenjem, antihipertenzivna terapija se uvodi kada su vrednosti arterijskog krvnog pritiska ≥ 140/90 mmHg, odnosno kada su u opsegu hipertenzije I stepena ukoliko je maligno oboljenje izlečeno, ukoliko lečenje malignog oboljenja još uvek traje i očekuje se izlečenje, ali i kada postoji diseminacija bolesti uz očekivano preživljavanje duže od tri godine (klasa preporuka I) [6]. Kod pacijenata sa metastatskim promenama i očekivanim preživljavanjem između jedne i tri godine vrednosti arterijskog krvnog pritiska u opsegu hipertenzije I stepena treba razmotriti kao prihvatljive (klasa preporuka IIa), a iste vrednosti arterijskog krvnog pritiska se mogu razmotriti i kod pacijenata sa lošom prognozom i očekivanim preživljavanjem kraćim od godinu dana (klasa preporuka IIb). Ciljne vrednosti arterijskog krvnog pritiska kod većine pacijenata sa onkohipertenzijom su < 140/90 mmHg (klasa preporuka I). Sa druge strane, mogu se razmotriti i vrednosti < 130/80 mmHg ukoliko pacijenti dobro tolerišu niže vrednosti pritiska, a posebno ako se radi o pacijentima sa visokim ili veoma visokim kardiovaskularnim rizikom (klasa preporuka IIb). Apsolutna indikacija za prekid antineoplastične terapije je hipertenzija III stepena (≥ 180/100 mmHg). Terapija se može nastaviti kada se vrednosti arterijskog krvnog pritiska snize ispod 160/100 mmHg, ali tada obavezno treba razmotriti smanjenje doze antineoplastičnih lekova [6].

Izbor antihipertenzivne terapije kod lečenja onkohipertenzije

Kod pacijenata sa hipertenzijom I stepena (< 160/100 mmHg) savetuje se antihipertenzivna monoterapija [6]. Prvu liniju terapije predstavljaju inhibitori angiotenzin-konvertujućeg enzima ili blokatori angiotenzinskih receptora, dok drugu liniju terapije čine dihidropiridinski kalcijumski antagonisti. Ukoliko su vrednosti arterijskog krvnog pritiska u opsegu hipertenzije II stepena, indikovana je kombinovana antihipertenzivna terapija. Primenjuje se kombinacija inhibitora sistema renin-angiotenzin-aldosteron i kalcijumskih antagonista u cilju ostvarivanja brze i efikasne kontrole hipertenzije. U slučaju rezistentne hipertenzije, treba razmotriti beta-blokatore (najpre vazodilatatorne, kao što su nebivolol i karvedilol), potom spironolakton, nitrate i hidralazin. Klasa lekova koju treba izbegavati kod onkoloških pacijenata su nedihidropiridinski kalcijumski antagonisti (verapamil i diltiazem). Iako nisu apsolutno kontraindikovani, istovremena primena sa lekovima

Target Blood Pressure Values in Onco-hypertension Management

In cancer patients, antihypertensive therapy is indicated when blood pressure values are ≥140/90 mmHg, that is, within grade 1 hypertension, if the malignancy is cured, if active cancer treatment is ongoing with curative intent, or in disseminated disease with an expected survival longer than three years (Class I recommendation) [6]. In patients with metastatic disease and expected survival between one and three years, grade 1 hypertension values may be considered acceptable (Class II recommendation). The same applies to patients with a poor prognosis and a life expectancy of less than 1 year (Class IIb recommendation). For most patients with onco-hypertension, target blood pressure values are <140/90 mmHg (Class I recommendation). On the other side, lower targets (<130/80 mmHg) may be considered if well tolerated, particularly in those with high or very high cardiovascular risk (Class IIb recommendation). Absolute indication for discontinuation of antineoplastic therapy is grade III hypertension (≥180/100 mmHg). Therapy may be resumed once blood pressure is reduced below 160/100 mmHg, with mandatory consideration of antineoplastic dose reduction [6].

Choice of Antihypertensive Therapy in Onco-hypertension

For patients with grade I hypertension (<160/100 mmHg), antihypertensive monotherapy is recommended [6]. First-line agents include angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, while dihydropyridine calcium channel blockers are considered second-line therapy. In grade II hypertension, combination therapy is indicated, typically involving a renin–angiotensin–aldosterone system inhibitor and a calcium channel blocker, to achieve rapid and effective blood pressure control. In resistant hypertension, beta-blockers (particularly vasodilating agents such as nebivolol and carvedilol), then spironolactone, nitrates, and hydralazine should be considered. The class of drugs to be avoided in oncology patients includes non-dihydropyridine calcium channel blockers (verapamil and diltiazem). Although not absolutely contraindicated, their concomitant use with VEGF-SPi agents carries the risk of worsening hypertension due to CYP3A4-mediated pharmacokinetic interactions and increased plasma concentrations of the antineoplastic drug [6].

Additional Factors Contributing to Onco-hypertension

In oncology patients, besides antineoplastic therapy, it's necessary to be aware that numerous associated

iz grupe VEGF-Spi nosi rizik od pogoršanja postojeće hipertenzije zbog interakcije na nivou metaboličkog sistema CYP3A4 u jetri i povećanja koncentracije antineoplastičnog leka u plazmi [6].

Pridruženi faktori koji doprinose onkohipertenziji

Pored antineoplastične terapije, kod onkoloških pacijenata je neophodno imati u vidu da postoje brojni pridruženi faktori koji mogu uticati na vrednosti arterijskog krvnog pritiska [23,24]. Tu spadaju komorbiditeti (npr. sekundarni depoziti u endokranijumu), konkomitantna terapija (kortikosteroidi koji se često primenjuju kao adjuvantna terapija ili nesteroidni antiinflamatorni lekovi primenjeni kao analgetici), bol, stres, anksioznost, poremećaj bubrežne funkcije (radijaciona nefropatija ili nefrotoksičnost antineoplastičnih lekova) i insuficijencija baroreceptora nakon radijacije u predelu vrata i grudnog koša. Takođe, i kod ovih pacijenata mogu postojati „efekat belog mantila“ i maskirana hipertenzija [23,24].

ZAKLJUČAK

Onkohipertenzija predstavlja novi oblik hipertenzije čija učestalost je u porastu, shodno porastu učestalosti onkoloških oboljenja, ali i razvoju novih antineoplastičnih lekova koji imaju svoje neželjene efekte na kardiovaskularni sistem. Za blagovremeno i adekvatno zbrinjavanje pacijenata sa onkohipertenzijom važno je dobro poznavanje kardiotoksičnih efekata antineoplastične terapije, ali je potrebno uzeti u obzir i stadijum onkološke bolesti i očekivano preživljavanje pacijenta kako bi se kod svakog pacijenta definisale ciljne vrednosti arterijskog krvnog pritiska. Otežavajuća okolnost u zbrinjavanju onkohipertenzije može biti istovremeno postojanje drugih kardiovaskularnih oboljenja koja povećavaju kardiovaskularni rizik, ali i drugih hroničnih oboljenja i pridruženih faktora koji mogu kompromitovati efekte primenjene antihipertenzivne terapije. Zbog svega navedenog, hipertenzija kod onkoloških pacijenata zahteva individualan i sveobuhvatan pristup koji je neophodno realizovati na svim nivoima zdravstvene zaštite, od ambulante nadležnog lekara opšte prakse do specijalizovanih tercijarnih zdravstvenih ustanova.

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factors can affect arterial blood pressure [23,24]. These include comorbidities (e.g., intracranial metastases), concomitant medications (such as corticosteroids used as adjuvant therapy or nonsteroidal anti-inflammatory drugs used for pain management), pain, stress, anxiety, renal dysfunction (radiation nephropathy or drug-induced nephrotoxicity), and baroreceptor insufficiency following neck or thoracic irradiation. Additionally, both "white coat effect" and masked hypertension may occur in these patients [23,24].

CONCLUSION

Onco-hypertension represents a novel and increasingly prevalent form of hypertension, reflecting the rising incidence of cancer and the development of new antineoplastic drugs, which have cardiotoxic potential. Timely and adequate management of patients with onco-hypertension requires a thorough understanding of the cardiotoxic effects of antineoplastic therapy, along with consideration of oncological disease stage and the patient's expected survival, to define individualized blood pressure targets. Management may be further complicated by concurrent cardiovascular diseases, additional chronic conditions, and factors that can compromise the efficacy of antihypertensive therapy. For all these reasons, hypertension in oncology patients demands an individualized and comprehensive approach that must be implemented at all levels of healthcare from primary care to specialized tertiary institutions.

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