

Research

Cite this article: Srikrajang S, Komolsuradej N, Chaovalit S, Chuaychoosakoon C. (2024) Effects of the WHO analgesic ladder on pain severity, pain interference, and blood pressure control in hypertensive patients with chronic musculoskeletal pain: a cross-sectional study. *Primary Health Care Research & Development* 25(e43): 1–9. doi: [10.1017/S1463423624000367](https://doi.org/10.1017/S1463423624000367)

Received: 3 December 2023

Revised: 16 May 2024

Accepted: 25 June 2024





Keywords:

general practice; hypertension; musculoskeletal; pain; WHO analgesic ladder

Corresponding author:

Narucha Komolsuradej;
Email: narucha.ko@psu.ac.th

Effects of the WHO analgesic ladder on pain severity, pain interference, and blood pressure control in hypertensive patients with chronic musculoskeletal pain: a cross-sectional study

Siwaluk Srikrajang¹ , Narucha Komolsuradej² , Sirawee Chaovalit¹  and Chaiwat Chuaychoosakoon³ 

¹Department of Physical Therapy, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand;

²Department of Family and Preventive Medicine, Prince of Songkla University, Songkhla, Thailand and ³Department of Orthopedics, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand

Abstract

Aim: This study aimed to investigate the effects of pain management according to the World Health Organization (WHO) analgesic ladder on pain severity, pain interference, and blood pressure (BP) in treated hypertensive patients with chronic musculoskeletal pain. **Background:** Pain management can affect BP control owing to the proposed mechanism by which persistent pain contributes to increased BP. However, there are inadequate studies investigating the benefit of pain management in controlling both pain and BP in hypertensive patients who have chronic pain. **Methods:** In this cross-sectional study, demographic data and pain characteristics (resting pain score on the numerical pain rating scale, pain severity, and pain interference subscale of the Brief Pain Inventory) were collected via face-to-face interviews. BP was measured thrice on the same day. Data on pain medications taken in the previous 1 month were retrieved from the medical records. Participants were categorized into three groups following pain management patterns according to the WHO analgesic ladder: no, partial, and complete treatment. Multivariate logistic regression analysis (MLRA) was used to analyse the association between the variables and uncontrolled BP. **Findings:** Among 210 participants, the mean (standard deviation) age was 68 (15.5) years, and 60.47% had uncontrolled BP. The resting pain score, pain severity, and pain interference subscale scores of the complete treatment group were significantly lower than that of the partial treatment group ($P = 0.036$, 0.026 , and 0.044 , respectively). The MLRA revealed that pain management patterns were associated with uncontrolled BP (adjusted odds ratio [AOR]: 6.75; 95% confidence interval [CI]: 2.71–16.78; $P < 0.001$) and resting pain scores (AOR: 1.17; 95% CI: 1.04–1.38; $P = 0.048$). Our findings suggest that pain management patterns adhering to the WHO analgesic ladder can reduce pain severity and pain interference and also control BP in hypertensive patients with chronic musculoskeletal pain.

Introduction

According to the World Health Organization (WHO), hypertension, a prevalent non-communicable disease worldwide, affects approximately 1.28 billion people aged 30–79 years (World Health Organization, 2023). Although preventable, this condition remains a significant cause of morbidity and mortality, particularly in older populations (Suol *et al.*, 2023). Although controlling blood pressure (BP) is encouraged in hypertensive patients, one of every five patients continues to experience uncontrolled BP even with treatment (World Health Organization, 2023).

The prevalence of musculoskeletal pain is 40–60% in older populations (Li *et al.*, 2022; Welsh *et al.*, 2020) and contributes to increased disability (Rundell *et al.*, 2019), psychosocial impairment (Karttunen *et al.*, 2012), and sleep disturbances (Chen *et al.*, 2011). Chronic musculoskeletal pain coexists with other chronic diseases, including hypertension (Bae *et al.*, 2015; Saccò *et al.*, 2013). Approximately 31.3%–39% of individuals with musculoskeletal pain reportedly have hypertension, higher than individuals with no pain (21–25.8%) both in clinical settings and the general community (Bruehl *et al.*, 2005; Giummarra *et al.*, 2020). Recent literature suggests a relationship between hypertension and pain (Alenazi & Alkhatami, 2023) due to decreased regulation of baroreflex activity (Saccò *et al.*, 2013). Although chronic pain may cause high BP (Bruehl *et al.*, 2018), most hypertension treatment guidelines focus on antihypertensive drugs and lifestyle modifications, focusing less on pain (Whelton *et al.*, 2018). Therefore, evidence regarding the impact of pain treatment strategies on BP control in hypertensive patients is lacking.

© The Author(s), 2024. Published by Cambridge University Press. This is an Open Access article, distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike licence (<http://creativecommons.org/licenses/by-nc-sa/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the same Creative Commons licence is used to distribute the re-used or adapted article and the original article is properly cited. The written permission of Cambridge University Press must be obtained prior to any commercial use.

Discussing pain management in primary care is challenging because of conflicting evidence regarding the management of multiple comorbidities (Krein *et al.*, 2007). However, the WHO proposed a standard recommendation for pain medication prescriptions, popularly known as the ‘WHO analgesic ladder’, an evidence-based framework recognized in pain management (Anekar, Hendrix, and Cascella, 2023). The analgesic ladder has demonstrated effectiveness and widespread usefulness in musculoskeletal disorders because it emphasizes individualized treatment plans based on pain intensity (El-Tallawy *et al.*, 2021). Previous studies have established that inappropriate pain management without regard to the WHO analgesic ladder can lead to persistent pain and unnecessary side effects (Ussai *et al.*, 2015), which highlighted the importance of this guideline for pain management in hypertensive patients in primary care. Therefore, this study aimed to investigate the impact of applying the WHO analgesic ladder on resting pain score, pain severity, pain interference, and BP control in treated hypertensive patients with chronic musculoskeletal pain. The findings of this study may reveal the pain management patterns that can simultaneously control pain and BP in this population.

Methods

Study design and setting

This cross-sectional study was conducted at the Primary Care Unit, the General Practitioner Outpatient Clinic, the Orthopaedics Clinic, and the Physical Therapy Clinic of Songklanagarind Hospital, Thailand, from 1 February to 31 May 2023. The study was advertised in the hospital area. The research protocol was approved by the Faculty of Medicine, Prince of Songkla University, Thailand (Code: REC.65-489-30-2). All patients provided written informed consent before enrolling in the study. Purposive sampling was used to select 210 participants who met the eligibility criteria. The inclusion criteria were as follows: (1) age ≥ 40 years, (2) diagnosis with primary hypertension for at least 3 months, (3) good compliance with hypertensive treatment, defined as regular intake of antihypertensive drugs without any treatment lapses in the previous 7 days, and (4) experiencing musculoskeletal pain lasting at least 3 months. The exclusion criteria were as follows: (1) experiencing pain from other sources within 24 h of data collection, such as headache or abdominal pain, (2) active cancer at any bodily site, (3) fractures in the area of pain location, (4) being bedridden, and (5) neurological deficits that affect walking ability.

The sample size was calculated with the n4studies application based on previous research focusing on the association between pain and BP using two independent proportions (Bruehl *et al.*, 2005). The proportion of hypertensive patients experiencing pain was set at 0.10, whereas those without pain were estimated at 0.26. The significance level (α error probability) was established at 0.05, and the β -error probability was set as 0.20. A sample size of 210 participants was subsequently determined.

Measurements and outcomes

BP measurements were performed by a trained physical therapist in a separate room using an autonomic BP monitor (TM-2657P; A&D Co. Ltd., Tokyo, Japan). The device was validated according to the British and Irish Hypertension Society standards (Chu *et al.*, 2023). After resting in a sitting position for at least 10 min, measurements were taken thrice at 1-min intervals. The mean of

the second and third values was used for data analysis. This BP assessment protocol was used in several settings in previous studies. The criteria for uncontrolled BP were systolic BP of ≥ 140 mmHg and/or diastolic BP of ≥ 90 mmHg (Olsen *et al.*, 2013; Wieberdink *et al.*, 2012).

Pain measurements were conducted using two tools for assessing the degree of pain through face-to-face interviews. Both pain assessments were administered to participants on the day of data collection and after at least 3 months of prescribed pain treatment. The first tool was the numerical pain rating scale (NPRS) to assess resting pain. Participants were asked to rate their resting pain on a scale of 0–10, with 0 denoting no pain and 10 representing the most imaginable pain. The second tool was the Thai version of the Brief Pain Inventory Short Form (BPI-SF), which comprises two subscales: pain severity and pain interference. The pain severity subscale score was derived from the mean of the participants’ current, worst, average, and least pain, experienced within a 24-h period. The pain interference subscale assesses seven functional aspects that pain may interfere with general activity, mood, walking ability, normal work, relationships with others, sleep, and enjoyment of life. The scores for each aspect range from 0 to 10, with 0 indicating no interference and 10 indicating complete interference due to pain. The mean scores across the seven aspects were calculated to measure overall pain interference (Komolsuradej *et al.*, 2023; Poquet & Lin, 2016).

Pain management data encompassing pain treatment prescriptions were extracted from the Hospital Information System (HIS), encompassing pain treatment prescriptions. The participants were categorized into three groups based on their pain management regimens following the WHO analgesic ladder, which comprises three hierarchical steps, each corresponding to the level of pain severity.

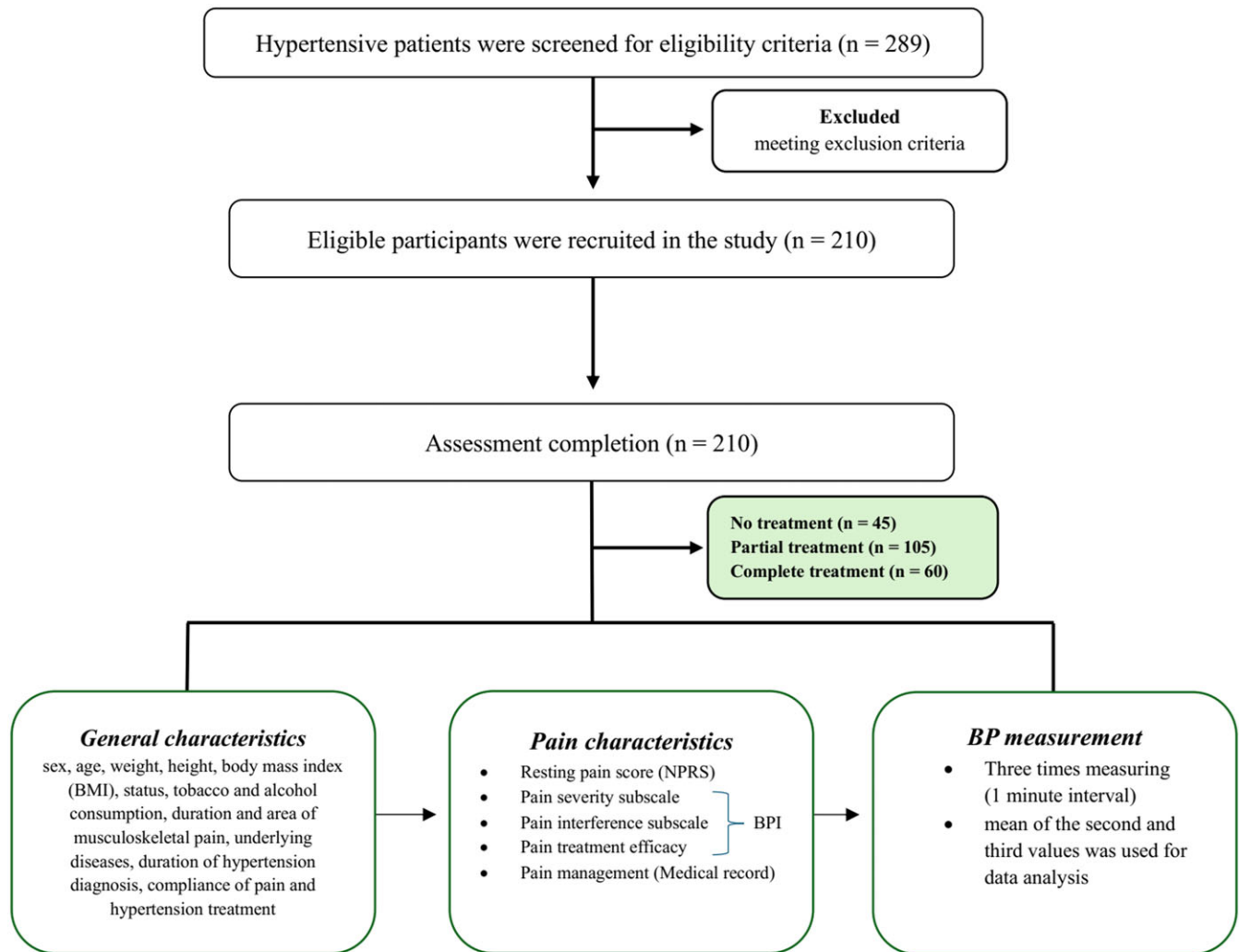
Step 1 involved the prescription of non-opioid analgesics, such as non-steroidal anti-inflammatory drugs (NSAIDs) and acetaminophen, for managing mild pain (NPRS score 1–4). Step 2 involved the administration of weak opioids, such as codeine or tramadol, in combination with non-opioid analgesics targeting moderate pain (NPRS score 5–6). Step 3 encompassed the prescription of strong opioids, such as morphine or fentanyl, for cases of severe pain (NPRS score 7–10) that remained uncontrolled despite weaker opioids (Hirschfeld & Zernikow, 2013; van Dijk *et al.*, 2012). In this study, ‘no treatment’ referred to not having received pain treatment in the previous month. ‘Partial treatment’ indicated pharmacological pain treatment below the recommended WHO analgesic ladder, whereas ‘complete treatment’ indicated pain treatment following the WHO analgesic ladder recommendation.

Procedure

The study was conducted using face-to-face interviews and retrospective data retrieved from the HIS. Participant information on general characteristics was collected using a standard questionnaire. Subsequently, the BPI-SF was used for pain evaluation, and BP was measured thrice. Finally, the history of pain treatment and drug prescriptions (type, time of consumption, and dose) within the previous 1 month was collected. The study flowchart is shown in Figure 1.

Statistical analysis

Data management was performed using R Studio Version 3.3.0 (Public Benefit Corporation, USA, 2009). The median, mean,



NPRS = Numerical pain rating scale
BPI = Brief Pain Inventory questionnaire

Figure 1. Flowchart of the hypertensive patients with chronic musculoskeletal pain participated in the study ($n = 210$).

interquartile range, standard deviation (SD), and percentage were calculated for descriptive analyses. The differences in pain characteristics, BP level, and associated factors among three pain management groups were evaluated using the Kruskal–Wallis test and analysis of variance F -test to compare continuous variables, whereas the chi-square and Fisher's exact test were used to compare categorical variables. Multivariate logistic regression analysis (MLRA) was used to analyse the association between the variables of interest and uncontrolled BP. The significance level was set at $P < 0.05$.

Results

Overall, 289 patients with hypertension were screened, and 210 had uncontrolled BP (60.48%). Of the participants, 62.4% ($n = 131$) were male. Most were older adults, aged > 60 years (79.5%), and all had at least one comorbidity (Table 1). There was a significant difference in the resting pain scores, pain severity subscale score, and pain interference subscale score among the pain management groups. Pain measurements reflected pain

characteristics following a minimum 3-month period of pain management. Across all pain aspects (resting pain, pain severity, and pain interference), the partial treatment group consistently exhibited higher pain levels, compared with the other groups. We found that pain interference was the most common pain characteristic, reflecting lower pain in the complete treatment group, compared with partial treatment and no treatment group ($P = 0.044$). The following pain interference items had the highest mean (SD): general activity (4.56 [3.01]), normal work (work outside the home and household chores) (4.00 [3.23]), and walking ability (3.53 [3.37]). Overall, 78.6% ($n = 105$) of participants received pain treatment, with most receiving partial treatment (63.4%) (Table 2).

According to the pain medication prescriptions, the most frequently prescribed NSAIDs were celecoxib, meloxicam, and etoricoxib. The most prescribed adjuvants comprised analgesic creams, anticonvulsants (gabapentin), and muscle relaxants (tolperisone) (Figure 2).

After identifying potential confounding variables, including age, sex, body mass index, underlying disease, hypertension

Table 1. Characteristics of participants according to pain management patterns according to WHO analgesic ladder (*n* = 210)

Factors	Pain management patterns according to WHO analgesic ladder			P-value
	No treatment (<i>n</i> = 45)	Partial treatment (<i>n</i> = 105)	Complete treatment (<i>n</i> = 60)	
Sex, <i>n</i> (%)				0.796
– Male	15 (33.3)	41 (39)	23 (38.3)	
– Female	30 (66.7)	64 (61)	37 (61.7)	
Age (year)				0.398
– age 40–60	6 (13.3)	23 (21.9)	14 (23.3)	
– age > 60	39 (86.7)	82 (78.1)	46 (76.7)	
BMI (kg/m ²), median (IQR)	25.5 (23.4, 27.5)	25.8 (22.2, 27.9)	24.1 (22.1, 28.2)	0.460
Comorbidity, <i>n</i> (%)				
– DM	12 (26.7)	25 (23.8)	17 (28.3)	0.804
– CVA	32 (71.1)	75 (71.4)	50 (83.3)	0.195
– DLP	10 (22.2)	32 (30.5)	14 (23.3)	0.400
– CKD	3 (6.7)	4 (3.8)	1 (1.7)	0.455
Marital status, <i>n</i> (%)				0.756
– Single	2 (4.4)	8 (7.7)	6 (10)	
– Married	38 (84.4)	78 (74.3)	43 (71.7)	
– Separate	5 (11.1)	19 (18.1)	11 (18.3)	
Education level, <i>n</i> (%)				0.079
– None/primary education	12 (26.7)	43 (41)	23 (38.3)	
– Secondary education	10 (22.2)	33 (31.4)	18 (30)	
– Bachelor's degree or higher	23 (51.1)	29 (27.7)	19 (31.7)	
Current smoking, <i>n</i> (%)				0.218
– Yes	0 (0)	6 (5.7)	1 (1.7)	
Current drinking, <i>n</i> (%)				0.399
– Yes	4 (8.9)	8 (7.6)	7 (11.7)	
Duration of hypertensive diagnosis (month), median (IQR)	84 (36, 120)	120 (60, 120)	108 (48, 120)	0.646
Duration of musculoskeletal pain (month), median (IQR)	12 (4, 48)	12 (6, 72)	18 (5, 39)	0.712
Compliance with pain treatment, <i>n</i> (%)				0.168
– Good compliance	38 (84.44)	78 (74.29)	41 (68.33)	
Pain location, <i>n</i> (%)				
– Neck	0 (0)	7 (6.67)	7 (11.66)	0.061
– Shoulder	11 (24.44)	18 (17.14)	8 (13.33)	0.331
– Upper back	4 (8.89)	4 (3.81)	3 (5.00)	0.441
– Lower back	11 (24.44)	29 (27.62)	18 (30.00)	0.821
– Hip & Thigh	3 (6.67)	9 (8.57)	5 (8.33)	0.923
– Knee	11 (24.44)	28 (26.67)	13 (21.67)	0.218
– Ankle & foot	5 (11.11)	10 (0.52)	6 (10.00)	0.957
Pain treatment efficiency (0–10)	7 (4,8)	7 (5,8)	6 (5,8)	0.542

Abbreviations: IQR, interquartile range; BMI, body mass index; DM, diabetes mellitus; CKD, chronic kidney disease; CVA, cerebral vascular accident; DLP, dyslipidaemia.

Table 2. Differences between pain characteristics (resting pain scale, pain severity subscale, and pain interference subscale) and BP among hypertensive patients (n = 210)

Variables	Pain management patterns according to WHO analgesic ladder			P-value
	No treatment (n = 45)	Partial treatment (n = 105)	Complete treatment (n = 60)	
<i>Pain characteristics</i>				
Resting pain score [mean (SD)]	5.0 (2.3)	5.7 (1.9)	5.1 (1.7)	0.036*
Pain severity subscale [mean (SD)]	3.9 (1.9)	4.6 (1.8)	4.0 (1.6)	0.026*
Pain interference subscale [median (IQR)]	3.0 (1.9, 4.3)	3.2 (1.9, 4.6)	2.1 (0.7, 4.3)	0.044*
<i>BP</i>				
Systolic BP [median (IQR)]	140.5 (130, 149.2)	138 (126, 151)	130 (123, 135)	< 0.001*
Diastolic BP [mean (SD)]	79.3 (12.4)	77.3 (11.8)	70.7 (10.6)	< 0.001*
Well-controlled BP [n (%)]	18 (40)	65 (43.33)	43 (71.67)	< 0.001*

*Statistically significant at $P < 0.05$ (analysed using the Kruskal-Wallis test or ANOVA F -test); SD, standard deviation; IQR, interquartile range.

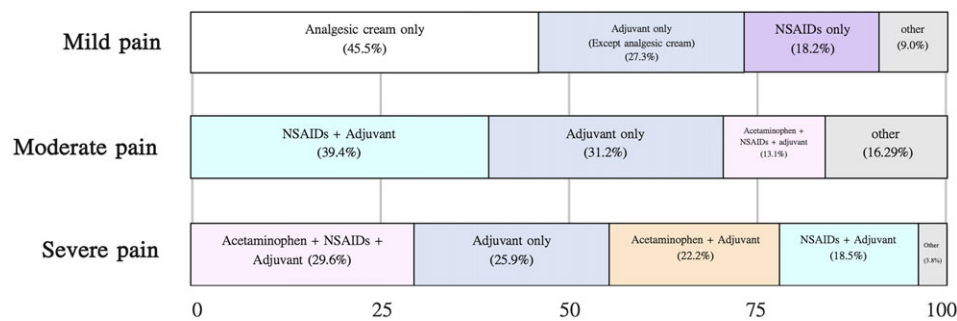


Figure 2. Pain medication prescriptions in patients receiving partial treatment following the WHO analgesic ladder with mild, moderate, and severe pain levels (n = 105) (NSAIDs, non-steroidal anti-inflammatory drugs).

treatment duration, and pain duration (Model 1 of three MLRA models), both the resting pain score and pain management were significantly associated with uncontrolled BP. The partial treatment group had the highest odds ratio for increased risk of uncontrolled BP ($P < 0.001$). However, variables such as pain severity, pain interference, area of pain, and treatment efficacy were not significantly associated with uncontrolled BP ($P > 0.05$) after conducting MLRA (Table 3).

Discussion

In this study, we found that adhering to the WHO analgesic ladder guidelines for pain treatment was associated with reduced pain severity, pain interference, and improved BP control. These findings demonstrate the benefits of the WHO analgesic ladder for controlling pain and BP in hypertensive patients with chronic musculoskeletal pain, particularly in older adults.

Our study findings suggest a positive association between pain and uncontrolled BP, which aligns with the result of a larger cohort study (n = 43, 789) that showed that hypertension was associated with pain severity (Giummarra *et al.*, 2020). Chronic musculoskeletal pain can cause various health problems that can be associated with uncontrolled BP, such as mood disorder and anxiety (Mazza *et al.*, 2016), sleep disturbance (Makarem *et al.*, 2021), decreased physical activity and movement limitation due to pain interference (Karayannis *et al.*, 2017) and lack of exercise adherence (Collado-Mateo *et al.*, 2021). Particularly, we found that comprehensive pain control can lower pain interference in hypertensive patients. The result of the three most occurring pain interference in this study, pain interference with general activity,

working, and walking abilities, suggests that chronic musculoskeletal pain decreased physical activity and movement in participants’ daily lives in this cohort. Several studies have also reported that reduced physical activity is associated with poorly controlled BP in treated hypertensive patients (Cherfan *et al.*, 2020; Solomon *et al.*, 2023; Zhang *et al.*, 2023). The pathophysiological mechanism between chronic musculoskeletal pain and hypertension can be attributed to physiological changes in the endogenous and cardiovascular pain regulatory systems (Olsen *et al.*, 2013; Saccò *et al.*, 2013). Even in acute pain, typically, the BP rises due to the autonomic response. However, chronic pain conditions often cause an opposite effect, resulting in a diminished baroreceptor response, possibly due to reduced vagal inhibitory activity (baroreceptor desensitization) (Bruehl *et al.*, 2002; Bruehl *et al.*, 2018). This failure in the baroreceptor homeostatic control mechanisms can lead to persistent BP elevation. Additionally, chronic pain can disrupt descending inhibitory pathways while facilitating nociceptive information transmission (Kosek & Ordeberg, 2000). This dual effect may intensify pain sensitivity and exacerbate BP elevation (Bruehl *et al.*, 2018; Rivasi *et al.*, 2022).

A significant association was observed between pain management patterns and uncontrolled BP in this study ($P < 0.001$). Notably, the complete treatment group exhibited a higher rate of well-controlled BP and significantly lower resting pain ($P = 0.036$), pain severity subscale ($P = 0.026$), and pain interference subscale ($P = 0.044$) scores than did the partial treatment group. Although theoretically supporting the possible physiological effect of pain and uncontrolled BP, a few clinical studies have demonstrated the evidence of this relationship. Among them, this study

Table 3. Multivariable logistic regression model for pain-related factors associated with uncontrolled BP in hypertensive patients with chronic pain ($n = 210$)

Variables	Model 1			
	Crude OR (95% CI)	Adjusted OR (95% CI)	P-value (Wald's test)	P-value (LR-test)
Groups of treatment			< 0.001	< 0.001*
– Complete treatment	5.54 (2.57, 11.93)	5.51 (2.46, 12.35)		
– Partial treatment	5.74 (2.46, 13.42)	6.75 (2.71, 16.78)		
Resting pain score	1.21 (1.05, 1.40)	1.17 (1.04, 1.38)	0.051	0.048*
Pain severity subscale score	1.17 (1.00, 1.37)	1.1 (0.92, 1.32)	0.283	0.283
Pain interference subscale score	1.05 (0.93, 1.18)	1.06 (0.95, 1.2)	0.305	0.304

* Statistically significant; CI, confidence interval; OR, odds ratio; LR, likelihood ratio.

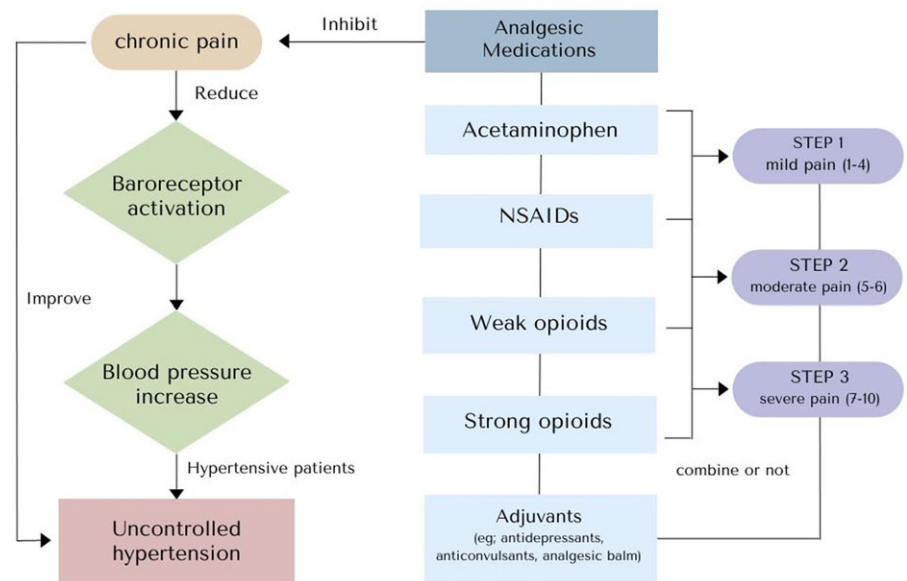


Figure 3. Effects of chronic pain and analgesic medications on blood pressure regulation (NSAIDs, non-steroidal anti-inflammatory drugs).

demonstrates the benefits of comprehensive pain management in positively improving BP control and alleviating pain, particularly pain interference. Studies have shown that pain interference is an important measurement due to its strong association with lower quality of life (Smith, Richardson, and Cowan, 2023), low conscientiousness (Judge, Meyr, and Segerstrom, 2021), and abnormal nutritional status in older adults (Komolsuradej *et al.*, 2023). Therefore, the lowest interference in the complete treatment group in this study may represent greater effects of pain control and can lead to reduced BP. This can be supported by experimental studies by Bruehl *et al.* that demonstrated a positive correlation of mean resting BP with pain severity level in patients with chronic benign pain (Bruehl, Burns, and McCubbin, 1998) and chronic low back pain (Bruehl *et al.*, 2002).

Regarding the drug responses, most patients in the complete treatment group experienced moderate pain. According to the WHO analgesic ladder recommendations (Figure 3), this group should receive weak opioids combined with non-opioid analgesics. Due to the potent histamine-mediated vasodilation effects of opioids and a hypersensitivity to opioid receptor agonists in hypertensive patients (Baldo and Pham, 2012), it could be speculated that opioids have a hypotensive effect (Zelis *et al.*, 1974), resulting in a decrease in BP in patients receiving opioids due to histamine-mediated vasodilation, which alleviates

hypotension (Chen and Ashburn, 2015). Furthermore, the hypotensive effects might be more significant in hypertensive patients due to their heightened sensitivity to opioid receptor agonists (Cozzolino *et al.*, 2005). In contrast, the most prevalent drug prescribed in the partial treatment group was NSAIDs combined with adjuvants. This treatment pattern can be attributed to increased BP because there is evidence that NSAIDs have the potential to increase BP by inhibiting prostaglandin synthesis and promoting the production of endothelin I (Snowden & Nelson, 2011), ultimately leading to increased secretion of aldosterone. This results in higher water retention with the sodium and calcium components (Morgan & Anderson, 2003), which may increase BP. Notably, the opioids tended not to be prescribed in this group, even for moderate pain. This may be explained by the physicians' intention to avoid potential adverse effects in older patients (Baldo & Pham, 2012; Krantz *et al.*, 2021). Moreover, 25.9–31.2% in the partial treatment group received adjuvant analgesics only, which may cause inadequate pain control and uncontrolled BP. However, we found a very low rate of non-pharmacological treatment prescriptions from physicians for pain control (5–10%), which correspond with a previous study that revealed low prevalence of non-pharmacological pain management in a specialized hospital due to factors such as limited access to pain assessment tools,

favourable attitude, and age of the attending healthcare personnel (Tsegaye *et al.*, 2023)

In managing hypertension in general practice, the latest treatment guideline, the European Society of Hypertension (ESH) guidelines (Mancia *et al.*, 2023), primarily focus on drug therapy and lifestyle modifications. Although there is growing recognition of the importance of pain control in hypertension management, current guidelines only specifically mention two diseases, gouty arthritis and rheumatoid arthritis, due to their association with cardiovascular risk. Interestingly, the guideline stated that treatment for these conditions, involving NSAIDs and glucocorticoids, can potentially interfere with hypertension treatment and lead to uncontrolled hypertension (Kremer *et al.*, 2009), as observed in our study where the high-dose NSAID group showed a higher incidence of uncontrolled hypertension.

The ESH 2023 guidelines emphasize the importance of managing simultaneous BP control and alleviating pain and inflammation but caution against excessive NSAID use (Hansildaar *et al.*, 2021). However, notably, previous guidelines, including the ESH 2017 and the American College of Cardiology and American Heart Association guidelines 2018, did not specify hypertension treatment in cases of chronic pain or musculoskeletal pain. Hence, there is an emerging trend suggesting that future treatment approaches should integrate both BP control and pain management (Williams *et al.*, 2018). This holistic approach potentially influences future treatment strategies in general practice for BP control in treated hypertensive patients who have chronic musculoskeletal pain, particularly in older adults.

Strengths and limitations

This is the first study to investigate the benefit of the WHO analgesic ladder in controlling pain severity, pain interference, and BP in hypertensive patients with chronic musculoskeletal pain. This study has some limitations. First, we were unable to compare changes in pain over the time course of medication consumption because the pain severity at the pre-visit used to determine treatment was assessed by a physician, which may have led to inconsistencies when compared with the pain measured by the researcher during the present visit. Second, only 5–10% of physician prescriptions included non-pharmacological therapies (such as physical therapy and acupuncture). As described previously, pain treatment appears beneficial for patients with high BP. Considering that non-pharmacological treatments could be an alternative for physicians to avoid the potential side effects of NSAIDs and opioid analgesics, their use may improve the efficacy of hypertensive treatment. Further studies are required to confirm these observations. Finally, this was an observational study (cross-sectional investigation with retrospective data retrieval), and further prospective studies are needed to determine the long-term effects of each pain medication on BP control.

Conclusions

The study findings support the effectiveness of comprehensive pain treatment following the WHO analgesic ladder in managing pain severity, pain interference, and BP in treated hypertensive patients. These results highlight the importance of incorporating pain control into the management of hypertension in primary care, especially for older individuals experiencing musculoskeletal pain.

Acknowledgements. Author would like to thank Kansupak Chinsunthia for data collection and Associate Professor Rassamee Chotipanvithayakul from Faculty of Medicine, Prince of Songkla University for her valuable advice throughout the study.

Financial statement. This study was supported by research grant from Faculty of Medicine, Prince of Songkla University (grant number MR PSU-653021-146).

Competing interests. None.

Ethical standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional guidelines on human experimentation (please name) and with the Helsinki Declaration of 1975, as revised in 2008. Written (or Verbal) informed consent was obtained from all subjects/patients.

References

- Alenazi AM and Alkhatami KM (2023) Hypertension is associated with joint pain severity among individuals with osteoarthritis. *Pain Management Nursing: Official Journal of the American Society of Pain Management Nurses* 24, e97–e101.
- Anekar A A, Hendrix J M and Cascella M (2023) *WHO Analgesic Ladder*. Treasure Island (FL): StatPearls Publishing.
- Bae YH, Shin JS, Lee J, Kim MR, Park KB, Cho JH and Ha IH (2015) Association between hypertension and the prevalence of low back pain and osteoarthritis in Koreans: a cross-sectional study. *PLoS One* 10, e0138790.
- Baldo BA and Pham NH (2012) Histamine-releasing and allergenic properties of opioid analgesic drugs: resolving the two. *Anaesthesia and Intensive Care* 40, 216–235.
- Bruhl S, Burns JW and McCubbin JA (1998) Altered cardiovascular/pain regulatory relationships in chronic pain. *International Journal of Behavioral Medicine* 5, 63–75.
- Bruhl S, Chung OY, Jirjis JN and Biridepalli S (2005) Prevalence of clinical hypertension in patients with chronic pain compared to nonpain general medical patients. *The Clinical Journal of Pain* 21, 147–153.
- Bruhl S, Chung OY, Ward P, Johnson B and McCubbin JA (2002) The relationship between resting blood pressure and acute pain sensitivity in healthy normotensives and chronic back pain sufferers: the effects of opioid blockade. *Pain* 100, 191–201.
- Bruhl S, Olsen RB, Tronstad C, Sevre K, Burns JW, Schirmer H, Nielsen CS, Stubhaug A and Rosseland LA (2018) Chronic pain-related changes in cardiovascular regulation and impact on comorbid hypertension in a general population: the Tromsø study. *Pain* 159, 119–127.
- Chen A and Ashburn MA (2015) Cardiac effects of opioid therapy. *Pain Medicine (Malden, Mass.)* 16, S27–31.
- Chen Q, Hayman LL, Shmerling RH, Bean JF and Leveille SG (2011) Characteristics of chronic pain associated with sleep difficulty in older adults: the maintenance of balance, independent living, intellect, and zest in the elderly (MOBILIZE) Boston study. *Journal of the American Geriatrics Society* 59, 1385–1392.
- Cherfan M, Vallée A, Kab S, Salameh P, Goldberg M, Zins M and Blacher J (2020) Unhealthy behaviors and risk of uncontrolled hypertension among treated individuals—The CONSTANCES population-based study. *Scientific Reports* 10, 1925.
- Chu RY, Dong D, Wong SY and Lee EK (2023) Barriers and determinants to the underutilized hypertension screening in primary care patients in Hong Kong: a mixed-method study. *International Journal of Environmental Research and Public Health* 20, 985.
- Collado-Mateo D, Lavín-Pérez AM, Peñacoba C, Del Coso J, Leyton-Román M, Luque-Casado A, Gasque P, Fernández-Del-Olmo MÁ and Amado-Alonso D (2021) Key factors associated with adherence to physical exercise in patients with chronic diseases and older adults: an umbrella review. *International Journal of Environmental Research and Public Health* 18, 2023.

- Cozzolino D, Sasso FC, Cataldo D, Gruosso D, Giammarco A, Cavalli A, Di Maggio C, Renzo G, Salvatore T, Giugliano D and Torella R (2005) Acute pressor and hormonal effects of beta-endorphin at high doses in healthy and hypertensive subjects: role of opioid receptor agonism. *The Journal of Clinical Endocrinology and Metabolism* **90**, 5167–5174.
- El-Tallawy SN, Nalamasu R, Salem GI, LeQuang JAK, Pergolizzi JV and Christo PJ (2021) Management of musculoskeletal pain: an update with emphasis on chronic musculoskeletal Pain. *Pain and Therapy* **10**, 181–209.
- Giummarra MJ, Tardif H, Blanchard M, Tonkin A and Arnold CA (2020) Hypertension prevalence in patients attending tertiary pain management services, a registry-based Australian cohort study. *PLoS one* **15**, e0228173.
- Hansildaar R, Vedder D, Baniaamam M, Tausche AK, Gerritsen M and Nurmohamed MT (2021) Cardiovascular risk in inflammatory arthritis: rheumatoid arthritis and gout. *The Lancet. Rheumatology* **3**, e58–e70.
- Hirschfeld G and Zernikow B (2013) Variability of “optimal” cut points for mild, moderate, and severe pain: neglected problems when comparing groups. *Pain* **154**, 154–159.
- Judge S, Meyr K and Segerstrom S (2021) Pain interference and conscientiousness in older adults. *Innov Aging* **5**, 889.
- Karayannis NV, Sturgeon JA, Chih-Kao M, Cooley C and Mackey SC (2017) Pain interference and physical function demonstrate poor longitudinal association in people living with pain: a PROMIS investigation. *Pain* **158**, 1063–1068.
- Karttunen N, Lihavainen K, Sipilä S, Rantanen T, Sulkava R and Hartikainen S (2012) Musculoskeletal pain and use of analgesics in relation to mobility limitation among community-dwelling persons aged 75 years and older. *European Journal of Pain (London, England)* **16**, 140–149.
- Komoluradej N, Srikrajang S, Rangsiprakarn N, Wongaree A, Wasusathapon C, Kanjanakomut D, Nukaew V, Cheutalay W, Kaewpipat S, Hoonthong S, Ung S and Iamthanaporn K (2023) The strong correlation between pain interference and abnormal nutritional status in older adults with chronic musculoskeletal pain. *Journal of Primary Care & Community Health* **14**, 21501319231174116.
- Kosek E and Ordeberg G (2000) Lack of pressure pain modulation by heterotopic noxious conditioning stimulation in patients with painful osteoarthritis before, but not following, surgical pain relief. *Pain* **88**, 69–78.
- Krantz MJ, Palmer RB and Haigney MCP (2021) Cardiovascular complications of opioid use: JACC state-of-the-art review. *Journal of the American College of Cardiology* **77**, 205–223.
- Krein SL, Heisler M, Piette JD, Butchart A and Kerr EA (2007) Overcoming the influence of chronic pain on older patients' difficulty with recommended self-management activities. *The Gerontologist* **47**, 61–68.
- Kremer JM, Bloom BJ, Breedveld FC, Coombs JH, Fletcher MP, Gruben D, Krishnaswami S, Burgos-Vargas R, Wilkinson B, Zerbini CA and Zwilllich SH (2009) The safety and efficacy of a JAK inhibitor in patients with active rheumatoid arthritis: results of a double-blind, placebo-controlled phase IIa trial of three dosage levels of CP-690,550 versus placebo. *Arthritis and Rheumatism* **60**, 1895–1905.
- Li CY, Lin WC, Lu CY, Chung YS and Cheng YC (2022) Prevalence of pain in community-dwelling older adults with hypertension in the United States. *Scientific Reports* **12**, 8387.
- Makarem N, Alcántara C, Williams N, Bello NA and Abdalla M (2021) Effect of sleep disturbances on blood pressure. *Hypertension (Dallas, Tex.: 1979)* **77**, 1036–1046.
- Mancia G, Kreutz R, Brunström M, Burnier M, Grassi G, Januszewicz A, Muiesan ML, Tsioufis K, Agabiti-Rosei E, Algharably EAE, Azizi M, Benetos A, Borghi C, Hitij JB, Cifkova R, Coca A, Cornelissen V, Cruickshank JK, Cunha PG, Danser AHJ, Pinho RM, Delles C, Dominiczak AF, Dorobantu M, Dumas M, Fernández-Alfonso MS, Halimi JM, Járαι Z, Jelaković B, Jordan J, Kuznetsova T, Laurent S, Lovic D, Lurbe E, Mahfoud F, Manolis A, Miglinas M, Narkiewicz K, Niiranen T, Palatini P, Parati G, Pathak A, Persu A, Polonia J, Redon J, Sarafidis P, Schmieder R, Spronck B, Stabouli S, Stergiou G, Taddei S, Thomopoulos C, Tomaszewski M, Van de Borne P, Wanner C, Weber T, Williams B, Zhang ZY and Kjeldsen SE (2023) 2023 ESH guidelines for the management of arterial hypertension the task force for the management of arterial hypertension of the European society of hypertension: endorsed by the international society of hypertension (ISH) and the European renal association (ERA). *Journal of Hypertension* **41**, 1874–2071.
- Mazza A, Ravenni R, Armigliato M, Rossetti C, Schiavon L, Fiorini F, Rigatelli G, Ramazzina E and Casiglia E (2016) Mood disorders in uncontrolled hypertension despite multiple anti-hypertensive medications: searching for a link. *High Blood Pressure & Cardiovascular Prevention: The Official Journal of the Italian Society of Hypertension* **23**, 41–46.
- Morgan T and Anderson A (2003) The effect of nonsteroidal anti-inflammatory drugs on blood pressure in patients treated with different antihypertensive drugs. *Journal of Clinical Hypertension (Greenwich, Conn.)* **5**, 53–57.
- Olsen RB, Bruehl S, Nielsen CS, Rosseland LA, Eggen AE and Stubhaug A (2013) Hypertension prevalence and diminished blood pressure-related hypoalgesia in individuals reporting chronic pain in a general population: the Tromsø study. *Pain* **154**, 257–262.
- Poquet N and Lin C (2016) The brief pain inventory (BPI). *Journal of Physiotherapy* **62**, 52.
- Rivasi G, Menale S, Turrin G, Coscarelli A, Giordano A and Ungar A (2022) The effects of pain and analgesic medications on blood pressure. *Current Hypertension Reports* **24**, 385–394.
- Rundell SD, Patel KV, Krook MA, Heagerty PJ, Suri P, Friedly JL, Turner JA, Deyo RA, Bauer Z, Nerenz DR, Avins AL, Nedeljkovic SS and Jarvik JG (2019) Multi-site pain is associated with long-term patient-reported outcomes in older adults with persistent back pain. *Pain Medicine (Malden, Mass.)* **20**, 1898–1906.
- Saccò M, Meschi M, Regolisti G, Detrenis S, Bianchi L, Bertorelli M, Pioli S, Magnano A, Spagnoli F, Giuri PG, Fiacadori E and Caiazza A (2013) The relationship between blood pressure and pain. *Journal of Clinical Hypertension (Greenwich, Conn.)* **15**, 600–605.
- Smith AV, Richardson EJ and Cowan R (2023) Pain interference, pain type, and quality of life among adults with spina bifida. *PM & R: The Journal of Injury, Function, and Rehabilitation* **16**, 586–593.
- Snowden S and Nelson R (2011) The effects of nonsteroidal anti-inflammatory drugs on blood pressure in hypertensive patients. *Cardiology in Review* **19**, 184–191.
- Solomon M, Negussie YM, Bekele NT, Getahun MS and Gurara AM (2023) Uncontrolled blood pressure and associated factors in adult hypertensive patients undergoing follow-up at public health facility ambulatory clinics in Bishoftu town, Ethiopia: a multi-center study. *BMC Cardiovascular Disorders* **23**, 258.
- Suol TP, Yen TND, Thanh VV, Hao YT and Thang N (2023) Medication use and adherence in patients with hypertension: a prospective study in Vietnam. *Journal of Health Science and Medical Research* **41**, e2023956.
- Tsegaye D, Yazew A, Gedfew M, Yilak G and Yalaw ZM (2023) Non-pharmacological pain management practice and associated factors among nurses working at comprehensive specialized hospitals. *SAGE open nursing* **9**, 23779608231158979.
- Ussai S, Miceli L, Pisa FE, Bednarova R, Giordano A, Della Rocca G and Petelin R (2015) Impact of potential inappropriate NSAIDs use in chronic pain. *Drug design, Development and Therapy* **9**, 2073–2077.
- van Dijk JF, Kappen TH, van Wijck AJ, Kalkman CJ and Schuurmans MJ (2012) The diagnostic value of the numeric pain rating scale in older postoperative patients. *Journal of Clinical Nursing* **21**, 3018–3024.
- Welsh TP, Yang AE and Makris UE (2020) Musculoskeletal pain in older adults: a clinical review. *The Medical Clinics of North America* **104**, 855–872.
- Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW, MacLaughlin EJ, Muntner P, Ovbigele B, Smith SC, Spencer CC, Stafford RS, Taler SJ, Thomas RJ, Williams KA, Williamson JD and Wright JT (2018) 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American college of cardiology/american heart association task force on clinical practice guidelines. *Hypertension (Dallas, Tex.: 1979)* **71**, e13–e115.
- Wieberdink RG, Ikram MA, Hofman A, Koudstaal PJ and Breteler MM (2012) Trends in stroke incidence rates and stroke risk factors in Rotterdam, the Netherlands from 1990 to 2008. *European Journal of Epidemiology* **27**, 287–295.

- Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, Clement DL, Coca A, de Simone G, Dominiczak A, Kahan T, Mahfoud F, Redon J, Ruilope L, Zanchetti A, Kerins M, Kjeldsen SE, Kreutz R, Laurent S, Lip GYH, McManus R, Narkiewicz K, Ruschitzka F, Schmieder RE, Shlyakhto E, Tsioufis C, Aboyans V, Desormais I, De Backer G, Heagerty AM, Agewall S, Bochud M, Borghi C, Boutouyrie P, Brguljan J, Bueno H, Caiani EG, Carlberg B, Chapman N, Cifková R, Cleland JGF, Collet JP, Coman IM, de Leeuw PW, Delgado V, Dendale P, Diener HC, Dorobantu M, Fagard R, Farsang C, Ferrini M, Graham IM, Grassi G, Haller H, Hobbs FDR, Jelakovic B, Jennings C, Katus HA, Kroon AA, Leclercq C, Lovic D, Lurbe E, Manolis AJ, McDonagh TA, Messerli F, Muiesan ML, Nixdorff U, Olsen MH, Parati G, Perk J, Piepoli MF, Polonia J, Ponikowski P, Richter DJ, Rimoldi SF, Roffi M, Sattar N, Seferovic PM, Simpson IA, Sousa-Uva M, Stanton AV, van de Borne P, Vardas P, Volpe M, Wassmann S, Windecker S, Zamorano JL, Windecker S, Aboyans V, Agewall S, Barbato E, Bueno H, Coca A, Collet JP, Coman IM, Dean V, Delgado V, Fitzsimons D, Gaemperli O, Hindricks G, Iung B, Jüni P, Katus HA, Knuuti J, Lancellotti P, Leclercq C, McDonagh TA, Piepoli MF, Ponikowski P, Richter DJ, Roffi M, Shlyakhto E, Simpson IA, Sousa-Uva M, Zamorano JL, Tsioufis C, Lurbe E, Kreutz R, Bochud M, Rosei EA, Jelakovic B, Azizi M, Januszewics A, Kahan T, Polonia J, van de Borne P, Williams B, Borghi C, Mancia G, Parati G, Clement DL, Coca A, Manolis A, Lovic D, Benkhedda S, Zelveian P, Siostrzonek P, Najafov R, Pavlova O, De Pauw M, Dizdarevic-Hudic L, Raev D, Karpettas N, Linhart A, Olsen MH, Shaker AF, Viigimaa M, Metsärinne K, Vavlukis M, Halimi JM, Pagava Z, Schunkert H, Thomopoulos C, Páll D, Andersen K, Shechter M, Mercurio G, Bajraktari G, Romanova T, Trušinskis K, Saade GA, Sakalyte G, Noppe S, DeMarco DC, Caraus A, Wittekoek J, Aksnes TA, Jankowski P, Polonia J, Vinereanu D, Baranova EI, Foscoli M, Dikic AD, Filipova S, Fras Z, Bertomeu-Martínez V, Carlberg B, Burkard T, Sdiri W, Aydogdu S, Sirenko Y, Brady A, Weber T, Lazareva I, Backer T, Sokolovic S, Jelakovic B, Widimsky J, Viigimaa M, Pörsti I, Denolle T, Krämer BK, Stergiou GS, Parati G, Trušinskis K, Miglinas M, Gerdtts E, Tykarski A, de Carvalho Rodrigues M, Dorobantu M, Chazova I, Lovic D, Filipova S, Brguljan J, Segura J, Gottsäter A, Pechère-Bertschi A, Erdine S, Sirenko Y and Brady A (2018) 2018 ESC/ESH guidelines for the management of arterial hypertension. *European Heart Journal* **39**, 3021–3104.
- World Health Organization (2023) *Hypertension*. Geneva: WHO.
- Zelis R, Mansour EJ, Capone RJ and Mason DT (1974) The cardiovascular effects of morphine. The peripheral capacitance and resistance vessels in human subjects. *The Journal of clinical investigation* **54**, 1247–1258.
- Zhang W, Xu R, Cai Z, Zheng X, Zheng M and Ni C (2023) Association between physical activity and resistant hypertension in treated hypertension patients: analysis of the national health and nutrition examination survey. *BMC Cardiovascular Disorders* **23**, 289.