MECHANISMS AND PHENOTYPES OF HYPERTENSION IN PATIENTS IN CHRONIC HEMODIALYSIS

NCT06764277

DATE: 09/11/2025

STUDY PROTOCOL

SALUD SECRETARÍA DE SALUD	Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán	INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN	

Title

Mechanisms and Phenotypes of Hypertension in Patients in Chronic Hemodialysis

Number

Clinical Trials.gov protocol NCT06764277.

Investigation type

Observational transversal studies of mechanisms, markers (diagnostic/predictive) and prevalence of phenotypes in patients in chronic hemodialysis
Population (one) 1 (categorized by severity of hypertension in 3 groups: normotensive, prehypertensive, hypertensive)
Study: Prospective, observational, unicentric, Open

Investigators

INVESTIGATOR	Institutional position	Role in the project	Telephone (ext.)	Correo-E
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Note. 2 new co-investigators added: Adolfo Díaz (Nephrology resident) and Brenda Delgado-Avila (nephrology resident

Investigators experience and role in the investigation

Investigator	Previous research experience
Dr. Bernardo Rodríguez Iturbe	Research experience in nephrology and hypertension
Dr. Ricardo Correa Rotter	Research Experience in nephrology and renal replacement therapy
Dra. Olynka Vega Vega	Research Experience in nephrology and renal replacement therapy
Dr. Eduardo Ríos Argaiz	Nephrology resident

Dra. Angeles Espinosa Cuevas	Research experience in bioimpedance

Institution

	Approved the project
Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán.	Yes (protocol NMM 4512-23-24-1

Sponsorships of other institutions

No _____

Payment to investigators (other than employment in the institution)

No .

Abstract/Summary

Title: Mechanisms and Phenotypes of Hypertension in Patients in Chronic Hemodialysis

Justification. Cardiovascular complications associated to arterial hypertension are critical determinants of the mortality of patients in chronic hemodialysis. Identification of the activity of the renin-angiotensin system and immune reactivity in association with water overload is of clinical importance because they are potentially treatable.

Aims. To examine systemic arterial blood pressure ambulatory blood pressure monitoring (ABPM) in the interdialytic period and its relation to the activity of the renin angiotensin system, immune reactivity and interdialytic weight gain in patients in chronic hemodialysis.

General design. Prospective study of a cohort of patients in the chronic hemodialysis program in the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán. Patients with the inclusion criteria will be evaluated with ABPM during the 24 hours in the interdialytic period. Weight, blood pressure, dialysis characteristics will be recorded. Blood samples will be obtained for hormonal determinations and immune reactivity at the end of the interdialytic period. Ultrasound will be used for determination of cardiac output and central venous pressure. Systemic vascular resistance will be calculated. Electric bioimpedance will be obtained would be obtained the first post dialysis day of the long interdialytic interval. *

- Note: bioimpedance was not obtained and was not part of the study

Background.

Chronic kidney disease (CKD) is associated with arterial hypertension (AHT). AHT is more frequent in renal vascular disease, diabetic nephropathy and polycystic kidney disease [1], the incidence of AHT in end stage CKD (eGFR<10ml/min/1.73m2) of any etiology is over 90% [2]. In CKD patients the etiology of AHT is multifactorial and sodium retention and volume expansion [3,4] , overactivity of the renin angiotensin system [5], proinflammatory immune reactivity [6-9], endothelin system [10,11], the sympathetic nervous system[12], secondary hyperparathyroidism[13], reduced kallikrein/kinin [14] and endothelial cell dysfunction and nitric oxide reduction[15], are known to play a role.

In the patient with end stage CKD, the most important prohypertensive factor is sodium and water retention with extracellular volume expansion that results in increase in cardiac output and peripheral vascular resistance[16]. For this reason, the universally accepted therapeutic measure is to attempt to keep in the so-called dry weight [17]. The determination of "dry weight" is controversial and in addition to absence of clinical signs of vascular congestion,

bioimpedance determinations have been used to estimate subclinical overhydration but its use has been associated with higher risk of dialysis hypotension and clinical determination of the lowest weight that is not associated with postural and dialysis hypotension or cramps and malnutrition [18,19,20].

With the emphasis placed in overhydration as a cause of AHT in end stage CKD, not enough attention has been placed to other factors which may play an important role especially because there is no predictable correlation between the severity of overhydration and the severity of hypertension, patients with normal blood pressure have significant overhydration and patients with bioimpedance-determined dry weight may

have significant hypertension. It is our rough estimate that in 85-90% of patients in chronic hemodialysis hypertension is associated to volume overload without predictable correlation and 10-15% of the patients have normal blood pressure despite various degrees of water overload.

The purpose of the study is to evaluate factors that may importantly contribute to hypertension in chronic dialysis patients; in particular, the renin-angiotensin system (RAAS)., the sympathetic nervous system and inflammatory immune reactivity. In relation to the RAAS, Neuman at al.[21], found that basal levels of angiotensin II are higher in patients with CKD than in normal controls, but the reduction resulting from with volume expansion is normal, indicating that physiologic responses are normal. We also know from the studies of Shalekamp et al.[22] that the activation of the renin-angiotensin system in CKD is not uniform and there are patients with normal and patients with high renin activity. In relation to inflammatory reactivity generated by autoimmune mechanisms, studies of several groups including ourselves [6.7,23,24] have established the inflammation in the arterial wall, in the central nervous system and in the kidney play an important pathogenic role by reducing vasodilatory responses that may be corrected with T regulatory cells[25], increasing the activity of the sympathetic nervous system [26-28], inhibiting pressure natriuresis[29] and stimulating sodium reabsorption[30, 31]. If these findings are shown in dialysis patients it is possible that anti-inflammatory treatment could have anti-hypertensive effects as it has been shown in experimental models and in patients[32].

An important aspect is the relationship between interdialytic weight gain and the phenotypes of arterial hypertension (sustained hypertension, diurnal and nocturnal hypertension, normal nocturnal dipping, non-dipping, exaggerated dipping and reverse dipping) that may be evaluated with ambulatory blood pressure monitoring (ABPM) [33] that are associated with worse prognosis [34,35]. Of interest, there are significant differences between ABPM and pre and post-dialysis blood pressure that are worthy to examine. and there is a high incidence of non-dippers in patients with CKD[36] and in patients with inflammation [37-39].

Hypothesis and research questions.

What is the relative importance of the renin-angiotensin system, the inflammatory immune reactivity and water overload in the interdialytic blood pressure in dialysis patients?

Working hypothesis: In patients in chronic dialysis the activity of the renin-angiotensin system and the inflammatory reactivity play a critical role in the severity of hypertension and in the absence of nocturnal dipping of blood pressure

Outcomes.

Primary Outcome :

Determine the relationship of blood pressure determined by ambulatory monitoring (ABPM) in the interdialytic period and the interdialytic weight gain and the levels of angiotensin II and inflammatory markers in patients in chronic dialysis.

Secondary Outcomes:

1) Determine the relationship of other parameters relevant to blood pressure pathophysiology with interdialytic weight gain and blood pressure
2) Evaluate the relationship between interdialytic weight gain, and other variables under study with hemodynamic parameters (systemic vascular resistance and cardiac output).
3) Evaluate differences between ABPM and dialysis blood pressure.

Methods. .

General

- Design of the study**:** One cohort. Observational prospective study.
- Patients: Patients in the chronic hemodialysis program in the Instituto Nacional de Ciencias Médicas y Nutrición “Salvador Zubirán” that meet the inclusion criteria and sign informed consent
- Date. abril 2023– junio 2024

- Days and hemodialysis and hemodialysis prescription will not be modified in the study. .
- Ambulatory blood pressure monitoring will be started after dialysis when the patient will be fitted with the equipment for ambulatory blood pressure monitoring and receive the instructions for its use.
- Blood simples (10 ml) will be taken at the end of the interdialytic period, (prior to the next dialysis) for the biomarkers under study.
- 1-2 hours after the end of dialysis the determination of cardiac output and central venous pressure determinations for calculation of the peripheral vascular resistance will be done by experts with experience in ultrasound methodology.

Methods

Hemodynamic determinations. Cardiac output will be measured by experts with experience by transthoracic echocardiography using ultrasound equipment Siemens Acuson P500 with convex transducer of 2-5Mhz and lineal transducer of 7.5Mhz. Measurements will be done in the 4th intercostal space at the mid clavicular line. Cardiac output (systolic volume x heart frequency) will be determined by ultrasound doppler of the flow of the outlet of left ventricle and the aortic area.

Ambulatory blood pressure monitoring will be done with Space Lab ambulatory monitor (SpaceLabs Co) with cuffs appropriate for the patient's size starting after dialysis. Measurement will be programed to be taken every 30 minutes during the day and every hour when the patient goes to bed. The patient will bring the equipment to the hospital when he comes for the next dialysis.

Biometric Bioimpedance. It was impossible to coordinate bioimpedance determinations within one week of the studies and this part of the study was omitted.

Blood samples and laboratory determinations. Blood samples (10 ml) will be taken from the venous side of the vascular access before the beginning of dialysis (end of the interdialytic period) and allowed to coagulate at 2-4°C. Serum samples will be stored at -80°C until the time of assay. All determinations will be done in the research laboratory of the Dept. of Nephrology and Mineral Metabolism of the Instituto de Ciencias Medicas y Nutrición "Salvador Zubirán". Angiotensin II will be determined by ELISA (my BioSource Cat.# MBS703599); Norepinephrine by ELISA (ABCAM, Cat. # AB287789); Copeptin by ELISA (Bio-techne/NovusBiological, Cat, # NBP2-69822), TNFα by ELISA (Human TNF-alpha Quantikine HS ELISA, R&D systems, Cat.# HSTA00E). All laboratory determinations will be done following the instructions of the commercial supplier. Peripheral white cell counts were used to calculate the NMLR (neutrophils + monocytes /lymphocytes ratio) inflammation index.

Informed Consent.

Presented separately

Medical Intervention

None. Is an observational study.

Sample size

All the patients in the chronic hemodialysis program of the INCMNSZ that meet the inclusion criteria will be invited to participate.

Inclusion criteria

- 18 years of age or older
- More than 3 months in chronic dialysis
- Stable clinical conditions with no evidence of infection or treatment changes in the previous month

- Signed informed consent to participate in the study.

Exclusion Criteria

- Previous nephrectomy
- Participation of the patient in another clinical trial requiring interventional treatment
- Patients with prosthesis and pacemakers
- Incapacity of placement of ABPM or insufficient valid recordings
- Incomplete collection of data
- Voluntary withdrawing of informed consent

Statistical Analysis. .

Gaussian (normal) distribution will be evaluated with Kolmogorov-Smirnoff tests. Data will be expressed with mean and standard deviation or standard error of the mean and 95% confidence interval. Variables with not normal distribution will be expressed with median and interquartile range. Categorical variables will be expressed as frequencies and percentages. Comparisons between two groups with normal distribution will be done with t tests and between several groups with one way ANOVA with Tukey post-tests. Comparisons in groups that do not have a normal distribution will be done with Kruskal-Wallis tests. Correlations will be explored with Pearson (data with normal distribution) or Spearman (data with not normal distribution). Normality of log2 data distribution will be explored when obtained data do not fit with a normal distribution. Statistical calculations will be done with software STATA (Statistic Data Analysis version 14.1 or with Graphpad 10 program. Two-tail p values <0.05 will be considered significant.

Groups.

There is one population of patients and for the purpose of some analyses, patients will be categorized in 3 groups by their mean ambulatory systolic blood pressure (ABP-SBP) : 1. ABP-SBP <130 mmHg (normotensives); 2) ABP-SBP 130-139 mmHg (prehypertensives) and 3) ≥140 mmHg (hypertensives)

Mechanisms for assignation of treatments.

There will be no treatment assigned as part of the study

Recruitment potential

We aim to recruit all patients that meet the inclusion criteria. Our estimate is 40-45 patients from a total of 50-55 in the chronic hemodialysis program of the INCMNSZ.

Recruitment incentives.

There will be no incentives.

Therapy

There will be no therapy as part of the study. Treatment received by the patient will not be modified.

Retirement of participants

Premature retirement of a participant could occur at the patient's request or by the unexpected development of fever or adverse event during the study. Cause of retirement will be duly recorded

Samples, administration and monitoring of the study.

Samples will be used only for the purposes of the study. The study will be conducted or supervised by one of the investigators. Any adverse event will be immediately notified to the treatment physician. Investigates will meet every month to discuss the progress of the study.

Methods of contacting the participants

Patients will be contacted when they come to their regular hemodialysis treatment. As specified in the informed consent, the patients will have telephone access to the following investigators +52.19991490061

(Dr. Rodríguez-Iturbe), +52.15579597066 (Ricardo Correa-Rotter), +52.5518437638, (Dr. Eduardo Ríos Argaiz)

Risks.

This is an observational study that does not include invasive studies. The patient will receive explanation on the procedure of ABPM. Ultrasound studies are routinely used in patients in chronic dialysis

Expected benefits.

There will be no direct benefits for the patient. Knowledge of heart function and hypertension phenotype may have indirect benefits for the indication of treatment by his/her treatment physician to whom the results of the study will be available. The patient will not be charged by any of the studies

References

1. Ridao, N., Luño, J., García de Vinuesa, S., Gómez, F., Tejedor, A., & Valderrábano, F. (2001). Prevalence of hypertension in renal disease. *Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association*, *16 Suppl 1*, 70–73. https://doi.org/10.1093/ndt/16.suppl_1.70
2. Buckalew Jr, V. M., Berg, R. L., Wang, S. R., Porush, J. G., Sally, R., Schulman, G., & Modification of Diet in Renal Disease Study Group. (1996). Prevalence of hypertension in 1,795 subjects with chronic renal disease: the modification of diet in renal disease study baseline cohort. *American Journal of Kidney Diseases*, *28*(6), 811-821.
3. Saad, E., Charra, B., & Raj, D. S. (2004). Hypertension control with daily dialysis. *Seminars in dialysis*, *17*(4), 295–298. https://doi.org/10.1111/j.0894-0959.2004.17330.x
4. Kim, K. E., Onesti, G., Schwartz, A. B., Chinitz, J. L., & Swartz, C. (1972). Hemodynamics of hypertension in chronic end-stage renal disease. *Circulation*, *46*(3), 456–464. https://doi.org/10.1161/01.cir.46.3.456
5. Neumann, J., Ligtenberg, G., Klein, I. I., Koomans, H. A., & Blankestijn, P. J. (2004). Sympathetic hyperactivity in chronic kidney disease: pathogenesis, clinical relevance, and treatment. *Kidney international*, *65*(5), 1568–1576. https://doi.org/10.1111/j.1523-1755.2004.00552.x
6. Rodriguez-Iturbe, B., Pons, H., & Johnson, R. J. (2017). Role of the Immune System in Hypertension. *Physiological reviews*, *97*(3), 1127–1164. https://doi.org/10.1152/physrev.00031.2016
7. McMaster, W. G., Kirabo, A., Madhur, M. S., & Harrison, D. G. (2015). Inflammation, immunity, and hypertensive end-organ damage. *Circulation research*, *116*(6), 1022–1033. https://doi.org/10.1161/CIRCRESAHA.116.303697
8. Mikolajczyk, T. P., Szczepaniak, P., Vidler, F., Maffia, P., Graham, G. J., & Guzik, T. J. (2021). Role of inflammatory chemokines in hypertension. *Pharmacology & therapeutics*, *223*, 107799. https://doi.org/10.1016/j.pharmthera.2020.107799

9. Rodriguez-Iturbe, B., & Johnson, R. J. (2019). Genetic Polymorphisms in Hypertension: Are We Missing the Immune Connection?. *American journal of hypertension*, *32*(2), 113–122. https://doi.org/10.1093/ajh/hpy168
10. McCoy, E. K., & Lisenby, K. M. (2021). Aprocitentan (a Dual Endothelin-Receptor Antagonist) for Treatment-Resistant Hypertension. *Journal of cardiovascular pharmacology*, *77*(6), 699–706. https://doi.org/10.1097/FJC.0000000000001023
11. Mallamaci, F., Parlongo, S., & Zoccali, C. (1993). Influence of cardiovascular damage and residual renal function on plasma endothelin in chronic renal failure. *Nephron*, *63*(3), 291–295. https://doi.org/10.1159/000187212
12. Ligtenberg, G., Blankestijn, P. J., Oey, P. L., Klein, I. H., Dijkhorst-Oei, L. T., Boomsma, F., Wieneke, G. H., van Huffelen, A. C., & Koomans, H. A. (1999). Reduction of sympathetic hyperactivity by enalapril in patients with chronic renal failure. *The New England journal of medicine*, *340*(17), 1321–1328. https://doi.org/10.1056/NEJM199904293401704
13. Raine, A. E., Bedford, L., Simpson, A. W., Ashley, C. C., Brown, R., Woodhead, J. S., & Ledingham, J. G. (1993). Hyperparathyroidism, platelet intracellular free calcium and hypertension in chronic renal failure. *Kidney international*, *43*(3), 700–705. https://doi.org/10.1038/ki.1993.100
14. Mitas, J. A., Levy, S. B., Holle, R., Frigon, R. P., & Stone, R. A. (1978). Urinary kallikrein activity in the hypertension of renal parenchymal disease. *The New England journal of medicine*, *299*(4), 162–165. https://doi.org/10.1056/NEJM197807272990402
15. Passauer, J., Pistrosch, F., Büssemaker, E., Lässig, G., Herbrig, K., & Gross, P. (2005). Reduced agonist-induced endothelium-dependent vasodilation in uremia is attributable to an impairment of vascular nitric oxide. *Journal of the American Society of Nephrology : JASN*, *16*(4), 959–965. https://doi.org/10.1681/ASN.2004070582
16. Kim, K. E., Onesti, G., Schwartz, A. B., Chinitz, J. L., & Swartz, C. (1972). Hemodynamics of hypertension in chronic end-stage renal disease. *Circulation*, *46*(3), 456–464. https://doi.org/10.1161/01.cir.46.3.456
17. Loutradis, C., Sarafidis, P. A., Ferro, C. J., & Zoccali, C. (2021). Volume overload in hemodialysis: diagnosis, cardiovascular consequences, and management. *Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association*, *36*(12), 2182–2193. https://doi.org/10.1093/ndt/gfaa182
18. Agarwal, R., & Weir, M. R. (2010). Dry-weight: a concept revisited in an effort to avoid medication-directed approaches for blood pressure control in hemodialysis patients. *Clinical journal of the American Society of Nephrology : CJASN*, *5*(7), 1255–1260.

https://doi.org/10.2215/CJN.01760210

19. Ohashi, Y., Sakai, K., Hase, H., & Joki, N. (2018). Dry weight targeting: The art and science of conventional hemodialysis. *Seminars in dialysis*, *31*(6), 551–556. https://doi.org/10.1111/sdi.12721
20. Agarwal, R., & Weir, M. R. (2010). Dry-weight: a concept revisited in an effort to avoid medication-directed approaches for blood pressure control in hemodialysis patients. *Clinical journal of the American Society of Nephrology : CJASN*, *5*(7), 1255–1260. https://doi.org/10.2215/CJN.01760210
21. Neumann, J., Ligtenberg, G., Klein, I. I., Koomans, H. A., & Blankestijn, P. J. (2004). Sympathetic hyperactivity in chronic kidney disease: pathogenesis, clinical relevance, and treatment. *Kidney international*, *65*(5), 1568–1576. https://doi.org/10.1111/j.1523-1755.2004.00552.x
22. Schalekamp, M. A., Schalekamp-Kuyken, M. P., de Moor-Fruytier, M., Meininger, T., Vaandrager-Kranenburg, D. J., & Birkenhäger, W. H. (1973). Interrelationships between blood pressure, renin, renin substrate and blood volume in terminal renal failure. *Clinical science and molecular medicine*, *45*(4), 417–428. https://doi.org/10.1042/cs0450417
23. Abais-Battad, J. M., Rudemiller, N. P., & Mattson, D. L. (2015). Hypertension and immunity: mechanisms of T cell activation and pathways of hypertension. *Current opinion in nephrology and hypertension*, *24*(5), 470–474. https://doi.org/10.1097/MNH.0000000000000146
24. Guzik, T. J., Hoch, N. E., Brown, K. A., McCann, L. A., Rahman, A., Dikalov, S., Goronzy, J., Weyand, C., & Harrison, D. G. (2007). Role of the T cell in the genesis of angiotensin II induced hypertension and vascular dysfunction. *The Journal of experimental medicine*, *204*(10), 2449–2460. https://doi.org/10.1084/jem.20070657
25. Barhoumi, T., Kasal, D. A., Li, M. W., Shbat, L., Laurant, P., Neves, M. F., Paradis, P., & Schiffrin, E. L. (2011). T regulatory lymphocytes prevent angiotensin II-induced hypertension and vascular injury. *Hypertension (Dallas, Tex. : 1979)*, *57*(3), 469–476. https://doi.org/10.1161/HYPERTENSIONAHA.110.162941
26. Carnevale, D., Pallante, F., Fardella, V., Fardella, S., Iacobucci, R., Federici, M., Cifelli, G., De Lucia, M., & Lembo, G. (2014). The angiogenic factor PlGF mediates a neuroimmune interaction in the spleen to allow the onset of hypertension. *Immunity*, *41*(5), 737–752. https://doi.org/10.1016/j.immuni.2014.11.002
27. Fay, K. S., & Cohen, D. L. (2021). Resistant Hypertension in People With CKD: A Review. *American journal of kidney diseases : the official journal of the National Kidney Foundation*, *77*(1), 110–121. https://doi.org/10.1053/j.ajkd.2020.04.017

28. Castañeda-Bueno, M., & Ellison, D. H. (2022). Blood pressure effects of sodium transport along the distal nephron. *Kidney international*, *102*(6), 1247–1258. https://doi.org/10.1016/j.kint.2022.09.009
29. Franco, M., Tapia, E., Bautista, R., Pacheco, U., Santamaria, J., Quiroz, Y., Johnson, R. J., & Rodriguez-Iturbe, B. (2013). Impaired pressure natriuresis resulting in salt-sensitive hypertension is caused by tubulointerstitial immune cell infiltration in the kidney. *American journal of physiology. Renal physiology*, *304*(7), F982–F990. https://doi.org/10.1152/ajprenal.00463.2012
30. Norlander, A. E., Saleh, M. A., Kamat, N. V., Ko, B., Gnecco, J., Zhu, L., Dale, B. L., Iwakura, Y., Hoover, R. S., McDonough, A. A., & Madhur, M. S. (2016). Interleukin-17A Regulates Renal Sodium Transporters and Renal Injury in Angiotensin II-Induced Hypertension. *Hypertension (Dallas, Tex. : 1979)*, *68*(1), 167–174. https://doi.org/10.1161/HYPERTENSIONAHA.116.07493
31. Rodriguez-Iturbe, B., & Johnson, R. J. (2010). The role of renal microvascular disease and interstitial inflammation in salt-sensitive hypertension. *Hypertension research : official journal of the Japanese Society of Hypertension*, *33*(10), 975–980. https://doi.org/10.1038/hr.2010.148
32. Rodriguez-Iturbe B. (2016). Autoimmunity in the Pathogenesis of Hypertension. *Hypertension (Dallas, Tex. : 1979)*, *67*(3), 477–483. https://doi.org/10.1161/HYPERTENSIONAHA.115.06418
33. Sorof, J. M., Brewer, E. D., & Portman, R. J. (1999). Ambulatory blood pressure monitoring and interdialytic weight gain in children receiving chronic hemodialysis. *American journal of kidney diseases : the official journal of the National Kidney Foundation*, *33*(4), 667–674. https://doi.org/10.1016/s0272-6386(99)70217-9
34. Cheng, Y., Li, Y., Zhang, F., Zhu, J., Wang, T., Wei, M., Mo, L., & Li, Y. (2020). Interdialytic blood pressure variability and the risk of stroke in maintenance hemodialysis patients. *Medicine*, *99*(29), e21232. https://doi.org/10.1097/MD.0000000000021232
35. Aslam, N., Missick, S., & Haley, W. (2019). Ambulatory Blood Pressure Monitoring: Profiles in Chronic Kidney Disease Patients and Utility in Management. *Advances in chronic kidney disease*, *26*(2), 92–98. https://doi.org/10.1053/j.ackd.2019.02.001
36. Cho, S. M. J., Lee, H., Yoo, T. H., Jhee, J. H., Park, S., & Kim, H. C. (2021). Association Between Nocturnal Blood Pressure Dipping and Chronic Kidney Disease Among Patients With Controlled Office Blood Pressure. *American journal of hypertension*, *34*(8), 821–830. https://doi.org/10.1093/ajh/hpab031
37. Kaya, M. G., Yarlioglues, M., Gunebakmaz, O., Gunturk, E., Inanc, T., Dogan, A., Kalay, N., & Topsakal, R. (2010). Platelet activation and inflammatory response in patients with non-dipper hypertension. *Atherosclerosis*, *209*(1), 278–282.

https://doi.org/10.1016/j.atherosclerosis.2009.09.010

38. von Känel, R., Jain, S., Mills, P. J., Nelesen, R. A., Adler, K. A., Hong, S., Perez, C. J., & Dimsdale, J. E. (2004). Relation of nocturnal blood pressure dipping to cellular adhesion, inflammation and hemostasis. *Journal of hypertension*, *22*(11), 2087–2093. https://doi.org/10.1097/00004872-200411000-00009
39. Tosu, A. R., Demir, S., Selcuk, M., Kaya, Y., Akyol, A., Ozdemir, M., & Tenekecioglu, E. (2014). Comparison of inflammatory markers in non-dipper hypertension vs. dipper hypertension and in normotensive individuals: uric acid, C-reactive protein and red blood cell distribution width readings. *Postepy w kardiologii interwencyjnej = Advances in interventional cardiology*, *10*(2), 98–103. https://doi.org/10.5114/pwki.2014.43514