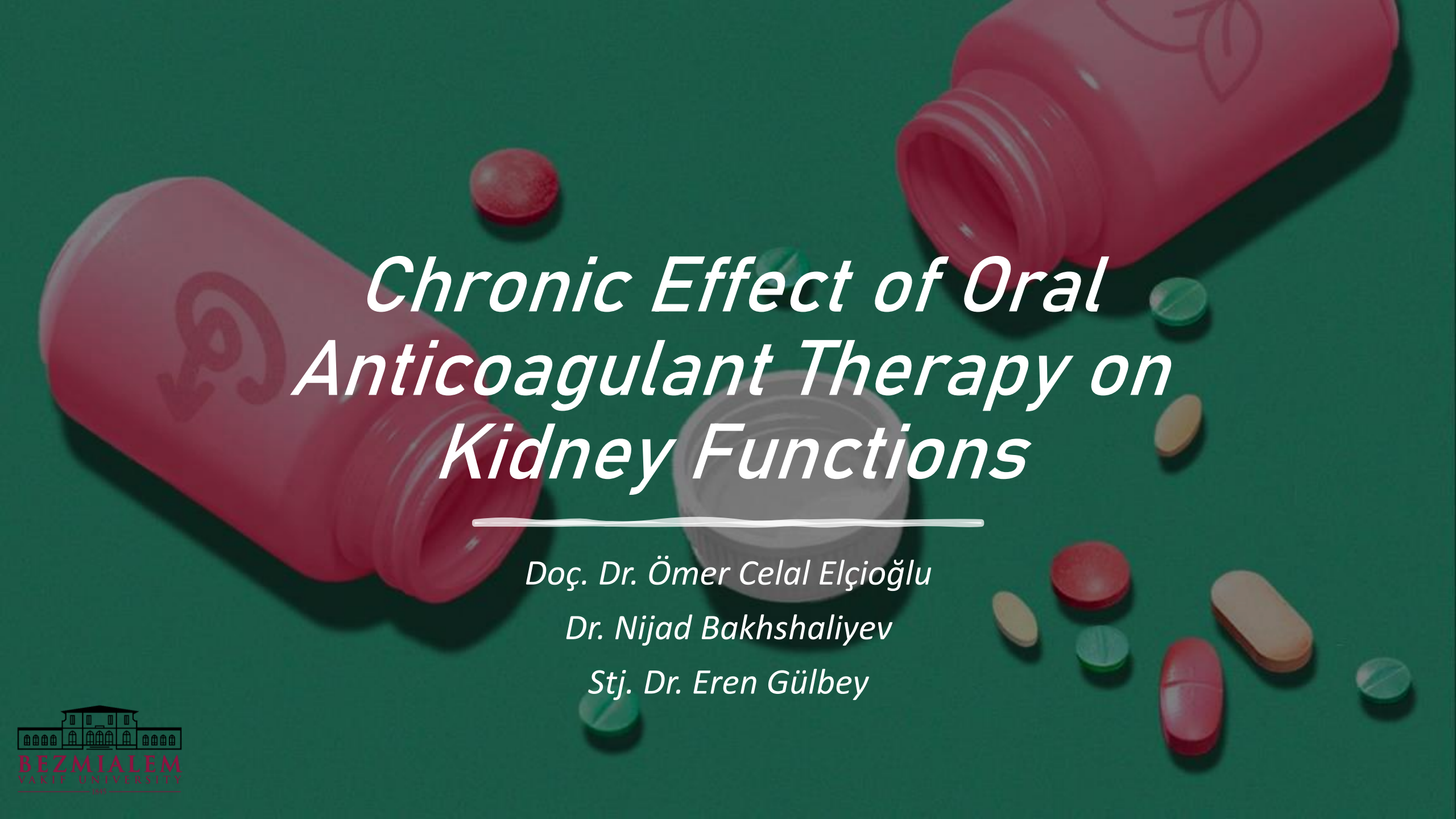


Chronic Effect of Oral Anticoagulant Therapy on Kidney Functions

Doç. Dr. Ömer Celal Elçioğlu

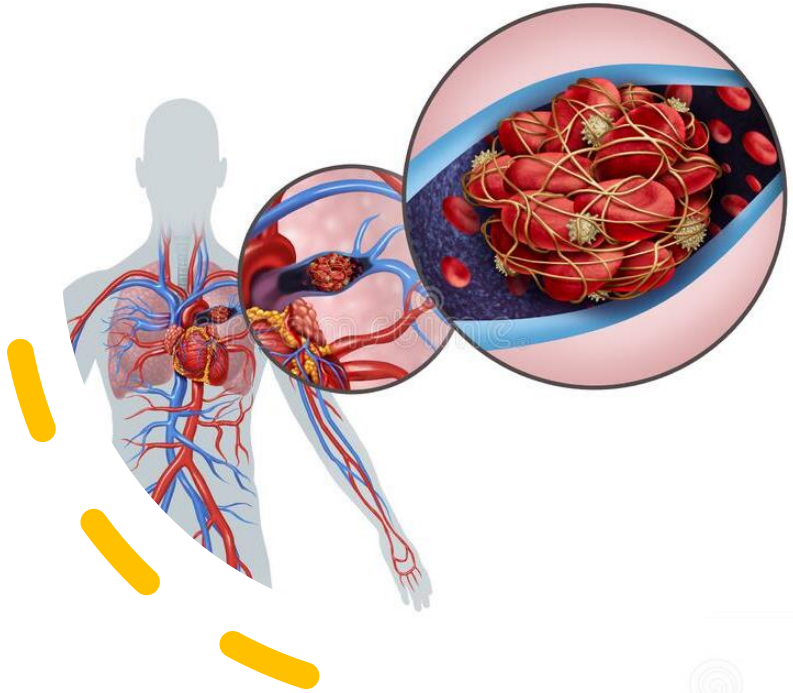
Dr. Nijad Bakhshaliyev

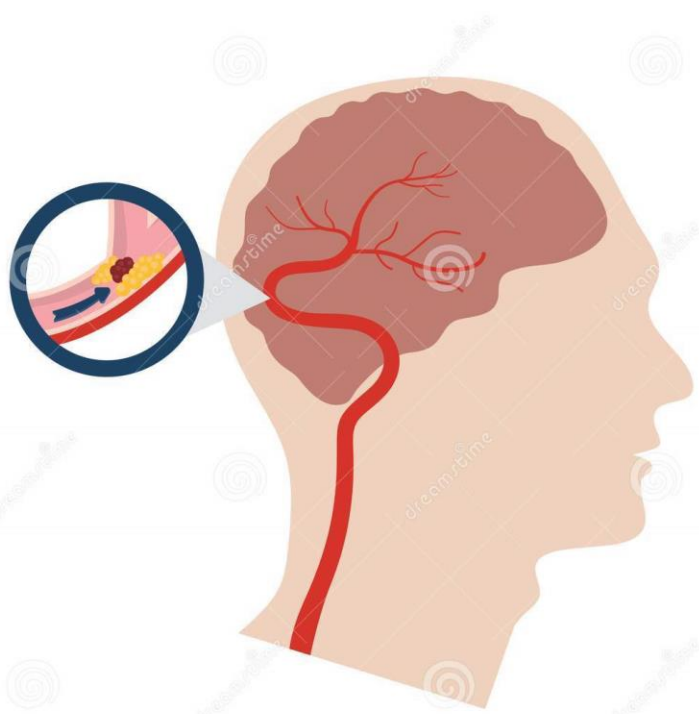
Stj. Dr. Eren Gülbey

BEZMIALEM VAKIF UNIVERSITY

INTRODUCTION

- Substances that prevent blood clotting.
- Prevents the formation of new thrombus and the expansion of existing thrombus.
- Oral and parenteral forms are available.
- Various anticoagulants are frequently used for therapeutic purposes and to reduce risks in patients with atrial fibrillation, patients with heart valves, patients with moderate and high stroke risk and systemic embolism.





BEZMIALEM VAKIF UNIVERSITY 1845

INTRODUCTION

- **Anticoagulant-associated nephropathy** is a newly understood form of acute kidney injury (AKI) due to oral anticoagulant use.
- It is also thought to cause progressive chronic kidney disease (CKD).
- Quite often in the use of anticoagulants in patients with AF.
- In a retrospective analysis, it was shown that the increase in serum creatinine seen within one week from the first time INR>3 (prothrombin time) of patients receiving warfarin therapy proves AKI.
- This damage was developed in 49.5% of the treated patients, 16.5% of the patients developed AKI without CKD, while 33% of the patients developed AKI on the existing CKD disease.

BEZMIALEM VAKIF UNIVERSITY 1845

References

1. Shin, JI., Secora, A., Alexander, GC., Inker, LA., Coresh, J., Chang, AR., & Grams, ME. (2018). Risks and Benefits of Direct Oral Anticoagulants across the Spectrum of GFR among Incident and Prevalent Patients with Atrial Fibrillation. *Clinical Journal of the American Society of Nephrology*, 13(8), 1144-1152.
2. Heine, GH., Brandenburg, V., Schirmer, SH. (2018). Oral Anticoagulation in Chronic Kidney Disease and Atrial Fibrillation. *Deutsches Arzteblatt International*, 115(17), 287-294.
3. Brodsky, S., Eikelboom, J., Hebert, LA. (2018). Anticoagulant-Related Nephropathy. *Clinical Journal of the American Society of Nephrology*, 29(12), 2787-2793.
4. Kumar, S., Lim, E., Covic, A., Verhamme, P., Gale, CP., Camm, AJ., Goldsmith, D. (2019). Anticoagulation in Concomitant Chronic Kidney Disease and Atrial Fibrillation. *Journal of the American Collage of Cardiology*, 74(17), 2204-2215.
5. Jain, N., Reilly, RF. (2018). Clinical Pharmacology of Oral Anticoagulants in Patients with Kidney Disease. *Clinical Journal of the American Society of Nephrology*, 14(2), 278-287.

AIM

In the literature, there are various studies on anticoagulant nephropathy, which has an acute effect of oral anticoagulant use, and studies on chronic damage to renal function due to long-term oral anticoagulant use **have been limited.**

Therefore, in our study, we aimed to observe whether the use of chronic oral anticoagulants has a negative long-term effect on renal function.

BEZMIALEM VAKIF UNIVERSITY 1845

METHODS / SUBJECTS

- The study was planned as a *retrospective study*
- Carried out with patients who have been followed up in Bezmialem Foundation University Hospital *Cardiology Polyclinic* between *1.1.2014 – 31.12.2021* and who have been indicated for oral anticoagulant drug use.
- Demographic data of patients were used.
- The parameters that used to evaluate kidney function and this research were mainly ***eGFR***, *creatinine* and *INR*.
- The minimum duration of oral anticoagulant use as *3 months* for patients were determined to be included in this study.

BEZMIALEM VAKIF UNIVERSITY 1845

METHODS / SUBJECTS

Two patient groups were generated.

Group 1 as one that receiving anticoagulants (n=102).

Group 2 as those not receiving anticoagulants (n=53).

The parameters related to these ***155 patients*** were collected over the duration of the patients' follow-up periods

BEZMIALEM VAKIF UNIVERSITY 1845

RESULTS

- When the groups receiving anticoagulants (group 1) (n=102) and those not receiving (group 2) (n=53) were compared, the mean age in the group receiving the drug was 74.23±10.24 years, while in the group not receiving the drug was 62.13±17.05 years, *(p<0.001)*.
- There was no significant difference between the two groups in terms of gender (34.3% male in group 1, 24.5% male in group 2) *(p=0.211)*.
- There was no difference between the two groups in terms of follow-up periods *(p=0.843)*, follow-up period = 4.3±2.4 years in group 1 and 4.28±2.57 years in group 2).

BEZMIALEM VAKIF UNIVERSITY 1845

RESULTS

- There was no significant difference in terms of first eGFR (estimated glomerular filtration rate) in both groups (*p=0.075*) (interquartile range for first eGFR in group 1=79.34 (69.70-88.17) and 89.11 (62.26-98.89) in group 2).
- ***However, delta eGFR (first eGFR-last eGFR) was significantly higher in group 1 (delta eGFR=16.89 (8.44-29.37) and 3.83 (1.89-7.74) for group 2) (p<0.001).***

BEZMIALEM VAKIF UNIVERSITY 1845

Linear Regression Model

- Since there was a significant difference between two groups in terms of the delta-eGFR (first eGFR value minus last eGFR) values, we evaluated the factors in relation to this difference.
- For all parameters, firstly, simple linear regression analysis was performed in terms of demographic data, concomitant diseases, medications and biochemical results (especially baseline values).
- Then, a multiple linear regression model was created using the parameters with significant results ($p<0.1$) in the simple linear regression analysis.

BEZMIALEM VAKIF UNIVERSITY 1845

Linear Regression Model

- Final multiple linear regression model revealed that treatment with an anti koagulan (warfarin or NOAC) (β=0.474, p=0.002), having hematuria (β=0.419, p=0.012), and last HbA1C level ((β=0.394, p=0.007) were related to the delta-eGFR level.
- The parameters that were found to be significantly correlated with delta eGFR in simple linear regression analysis but not in the multiple linear regression model were as follows; age of patients, diagnosis of atrial fibrillation or diabetes mellitus, use of beta-blockers or oral anti-diabetic drugs, presence of proteinuria, initial HbA1C value, mean HbA1C value, mean leukocyte values, mean urine pH value.

CONCLUSION

- According to the results and significance of delta eGFR, *it can be said that chronic anticoagulant use may have a negative effect on kidney function*.
- More detailed research with many more patients is needed to clarify this situation.

BEZMIALEM VAKIF UNIVERSITY 1845

ABSTRACT

- **Chronic Effect of Oral Anticoagulant Therapy on Kidney Functions**

- Eren Gülbey[1], Nijad Bakhshaliyev[2], Ömer Celal Elçioğlu[3]
- [1]Bezmialem Vakıf University, Faculty of Medicine, Istanbul, Turkey.
- [2] Bezmialem Vakıf University, Faculty of Medicine, Department of Cardiology, Istanbul, Turkey.
- [3] Bezmialem Vakıf University, Faculty of Medicine, Department of Nephrology, Istanbul, Turkey.

- **Introduction:** Oral anticoagulants are drugs that are used quite frequently today for therapeutic purposes and to reduce risks, especially in patients with atrial fibrillation (AF), with heart valves, with moderate and high stroke risk, and in systemic embolism. Recently, new types of oral anticoagulants that are not vitamin K antagonists have become available as an alternative to warfarin. In the literature, there are various studies on anticoagulant nephropathy, which has an acute effect of oral anticoagulant use, and studies on chronic damage to renal function due to long-term oral anticoagulant use have been limited. Therefore, we aimed to observe whether the use of chronic oral anticoagulants has a negative long-term effect on renal function.

- **Methods:** In this study, demographic data of patients were used. The parameters that used to evaluate kidney function and this research were mainly eGFR, creatinine and INR. Since the long-term effect of oral anticoagulant use on renal function were investigated, the minimum duration of oral anticoagulant use as 3 months for patients were determined to be included in this study. The study was planned as a retrospective study to be carried out with patients who have been followed up in Bezmialem Foundation University Hospital Cardiology Polyclinic between 1.1.2014 – 31.12.2021 and who have been indicated for oral anticoagulant drug use. Two patient groups were generated. One that receiving anticoagulants as group 1 (n=102). Group 2 as those not receiving anticoagulants (n=53). The parameters related to these 155 patients were collected over the duration of the patients' follow-up periods.

- **Results:** When the groups receiving anticoagulants (group 1) (n=102) and those not receiving (group 2) (n=53) were compared, the mean age in the group receiving the drug was 74.23±10.24 years, while in the group not receiving the drug was 62.13±17.05 years, ($p<0.001$). There was no significant difference between the two groups in terms of gender (34.3% male in group 1, 24.5% male in group 2) ($p=0.211$). There was no difference between the two groups in terms of follow-up periods ($p=0.843$), follow-up period = 4.3±2.4 years in group 1 and 4.28±2.57 years in group 2). There was no significant difference in terms of first eGFR (estimated glomerular filtration rate) in both groups ($p=0.075$) (interquartile range for first eGFR in group 1=79.34 (69.70-88.17) and 89.11 (62.26-98.89) in group 2). However, delta eGFR (first eGFR-last eGFR) was significantly higher in group 1 (delta eGFR=16.89 (8.44-29.37) for group 1 and 3.83 (1.89-7.74) for group 2) ($p<0.001$).

- **Linear Regression Model:** Since there was a significant difference between two groups in terms of the delta-eGFR (first eGFR value minus last eGFR) values, we evaluated the factors in relation to this difference. For all parameters, firstly, simple linear regression analysis was performed in terms of demographic data, concomitant diseases, medications and biochemical results (especially baseline values). Then, a multiple linear regression model was created using the parameters with significant results ($p<0.1$) in the simple linear regression analysis. Final multiple linear regression model revealed that treatment with an anti koagulan (warfarin or NOAC) ($\beta=0.474$, p=0.002), having hematuria ($\beta=0.419$, p=0.012), and last HbA1C level ($\beta=0.394$, p=0.007) were related to the delta-eGFR level. The parameters that were found to be significantly correlated with delta eGFR in simple linear regression analysis but not in the multiple linear regression model were as follows; age of patients, diagnosis of atrial fibrillation or diabetes mellitus, use of beta-blockers or oral anti-diabetic drugs, presence of proteinuria, initial HbA1C value, mean HbA1C value, mean leukocyte values, mean urine pH value.

- **Conclusion:** According to the results and significance of delta eGFR, it can be said that chronic anticoagulant use may have a negative effect on kidney function. More detailed research with many more patients is needed to clarify this situation.

- **Keywords:** Oral anticoagulant, kidney, eGFR, INR, Creatinine

BEZMIALEM VAKIF UNIVERSITY 1845

THANK YOU FOR YOUR PATIENCE…