

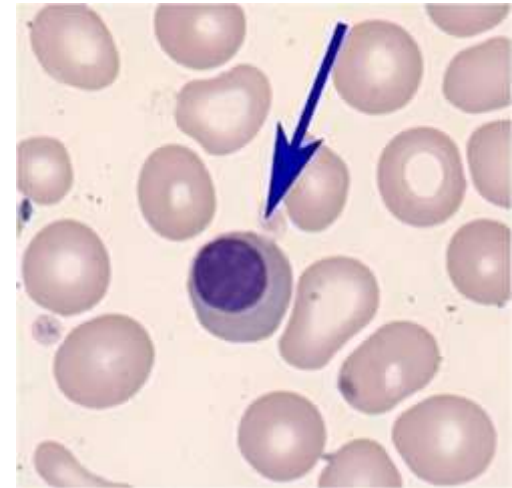


Kardiyovasküler Hastalıklarda Çekirdekli Kırmızı Kan Hücrelerinin Tanısal Değeri

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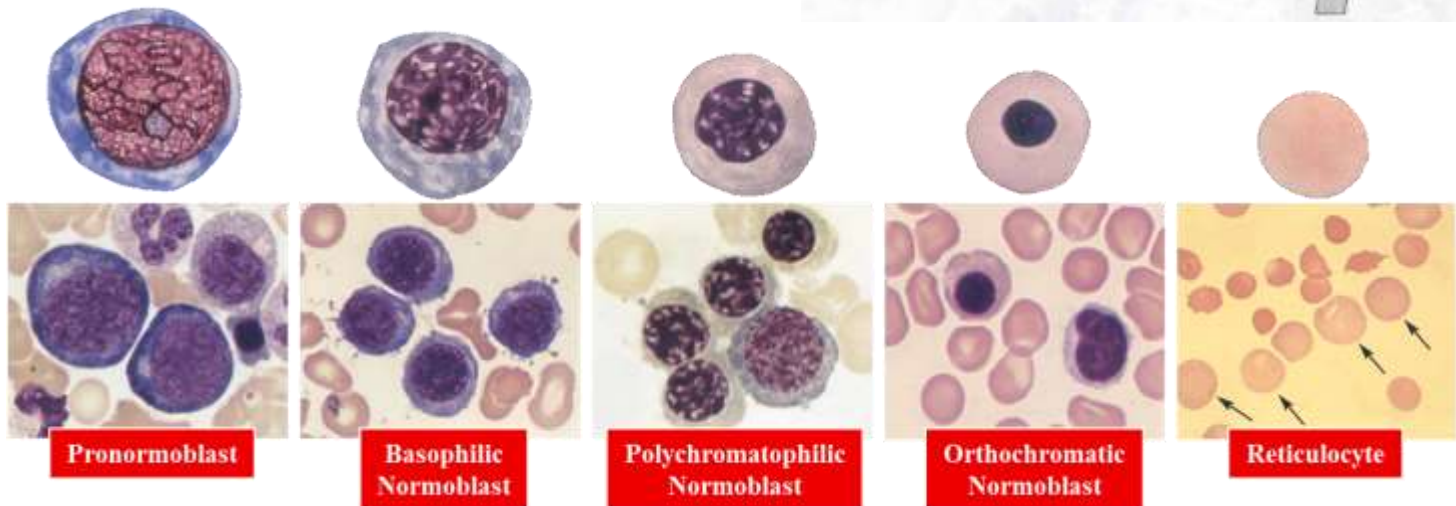
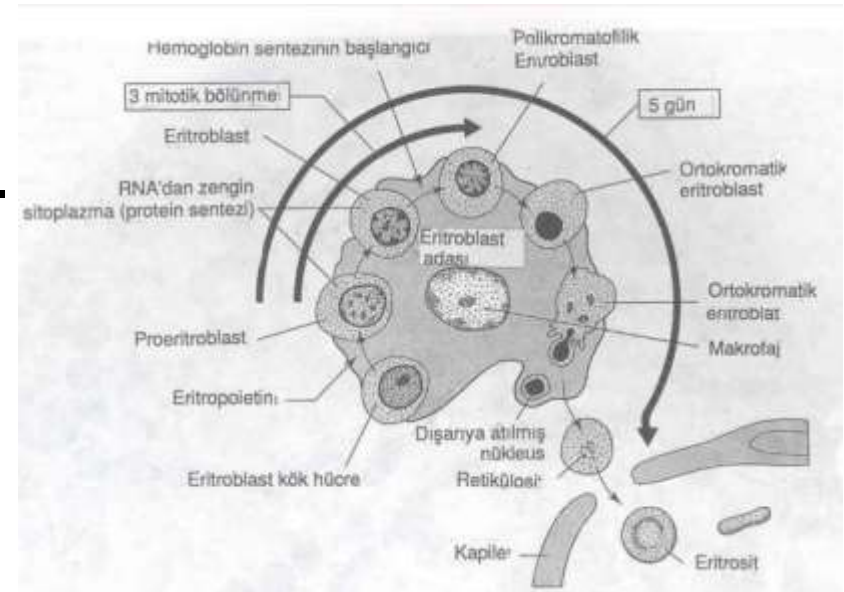
Sunum Planı

- Eritropoez ve Eritropoez Stimölasyonu
- Çekirdekli Kırmızı Kan Hücrelerin (ÇKKH) ve Hastalıklarla ilişkisi
- ÇKKH'nin kardiyovasküler hastalıklardaki yeri ve tanısal değeri
- ÇKKH'nin Cerrahi yoğun bakım hastalarında mortalite ile ilişkisi
- ÇKKH ve OUAS-hipotez



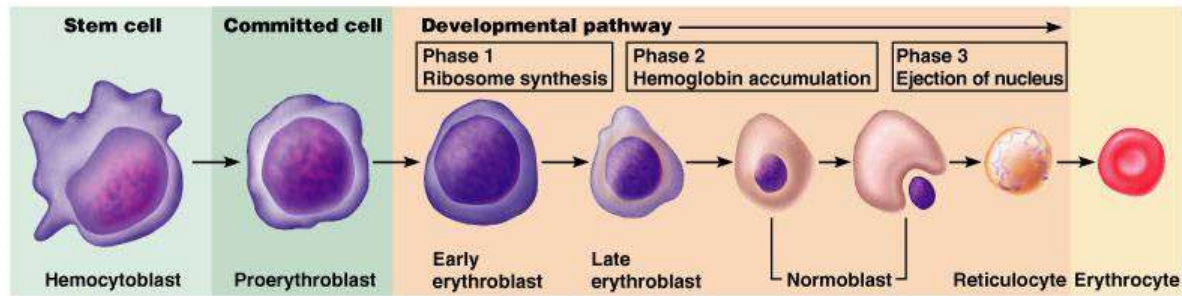
Eritropoez Nedir?

- Kemik iliğinden eritrositlerin yapımı olayına eritropoez denir.
- Başlıca gerekli bileşenler: eritropoetin ve sitokinlerdir (IL-3 ve IL- 6) .



Eritropoez Stimölasyonu

- Doku oksijenlenmesinin azalmasına neden olan faktörler eritropoezi arttırır:
 - Düşük kan hacmi
 - Anemi
 - Hemoglobin azlığı
 - Azalmış kan akımı
 - Solunum güçlüğü



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Çekirdekli Kırmızı Kan Hücrelerinin (ÇKKH) Periferik Kandaki Varlığı

- Yenidoğanda
 - Fetal oksijenizasyon ↓
 - Asfiksi
 - İdyopatik büyüme geriliği
 - Ensefalopati
 - Ductus arteriosus
 - Erken doğuma bağlı mortalite
 - Anneye bağlı sorunlar (obezite, HT, DM)
- Normal değil (erişkinde)
- Yanık
- Anemi (Talasemi, Orak hücre)
- Kanser

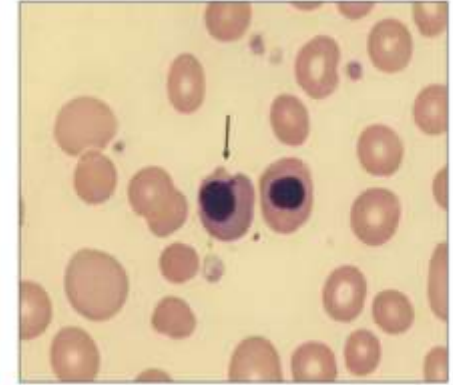


Figure 1: Nucleated red blood cells as seen in the peripheral smear of cord blood

Nucleated Red Blood Cells as Predictors of All-Cause Mortality in Cardiac Intensive Care Unit Patients: A Prospective Cohort Study.

Monteiro Júnior JG¹, Torres Dde O², da Silva MC², Ramos TM², Alves ML², Nunes Filho WJ¹, Damasceno EP¹, Brunet AF¹, Bittencourt MS³, Pedrosa RP¹, Sobral Filho DC¹.

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RESEARCH ARTICLE

Nucleated Red Blood Cells as Predictors of All-Cause Mortality in Cardiac Intensive Care Unit Patients: A Prospective Cohort Study

José Gildo de Moura Monteiro Júnior^{1*}, Dêlania de Oliveira Cipriano Torres², Maria Cleide Freire Clementino da Silva², Tadzia Maria de Brito Ramos², Marlene Lette Alves², Wellington Jorge Nunes Filho¹, Edgar Paulo Damasceno¹, Antônio Fernandes Brunet¹, Márcio Sommer Bittencourt³, Rodrigo Pinto Pedrosa¹, Dário Celestino Sobral Filho¹

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Abstract

Background

The presence of nucleated red blood cells (NRBCs) in the peripheral blood of critically ill patients is associated with a poorer prognosis, though data on cardiovascular critical care patients is lacking. The aim of the present study was to assess the role of NRBCs as a predictor of intensive care unit (ICU) and in-hospital all-cause mortality among cardiologic patients.



OPEN ACCESS

Citation: Monteiro Júnior JG, Torres Dde O, da Silva MC, Ramos TM, Alves ML, Nunes Filho WJ, et al. (2015) Nucleated Red Blood Cells as Predictors of All-Cause Mortality in Cardiac Intensive Care Unit

Hipotez:

Kardiyovasküler yoğun bakım ünitelerinde bulunan kötü prognozlu hastalarda ÇKKH'nin periferik kandaki varlığı bir belirteç olarak kullanılabilir mi?

[The occurrence of normoblasts in the peripheral blood in congestive heart failure: an indication of unfavorable prognosis.](#)

GROEN J. GODFRIED EG

Blood. 1948 Dec;3(12):1445-52. No abstract available.

PMID: 18893856

[Similar articles](#)

THE OCCURRENCE OF NORMOBLASTS IN THE PERIPHERAL BLOOD IN CONGESTIVE HEART FAILURE: AN INDICATION OF UNFAVORABLE PROGNOSIS

By J. GROEN, M.D., AND E. G. GODFRIED, M.D.

DURING THE PAST year the authors have observed 9 patients with severe congestive heart failure, all of whom showed a varying number of normoblasts in the peripheral blood. In some of these cases there was a temporary remission of the sequelae of the heart failure; during this remission the normoblasts disappeared from the peripheral blood. However, in all cases the patients died.

CASE REPORTS

Case 1. C. D., a 34 year old woman, was admitted on June 11, 1946, because of decompensated mitral stenosis. She was slightly jaundiced; the liver was greatly enlarged; there were infarcts in both lungs. Five per cent normoblasts were found in the peripheral blood. The patient died on July 2, 1946. The diagnosis was confirmed at autopsy.

Case 2. S. W., a 56 year old woman, entered the hospital on May 9, 1946, because of dyspnea, from which she had been suffering during the previous six months. She was cyanotic, dyspneic, and had slight jaundice. On examination, a mitral insufficiency, stenosis and auricular fibrillation were found. The liver was much enlarged; there was extensive edema. During this period, 10 and 17 per cent, respectively, of normoblasts were found on two occasions in the peripheral blood, but these disappeared within three days when her condition improved. In spite of this remission, the patient died on May 21, 1946. On the day before her death she had another infarction of the lung.

On May 11, a sternal puncture had been performed. The bone marrow was found to be essentially normal, but the presence of a relatively great number of normoblasts and erythroblasts was noted (about 25 per cent of all nucleated cells).

The diagnosis of valvular heart disease was confirmed at autopsy; there were many infarcts in both lungs and a thrombosis of the left auricle of the heart.

Case 3. A. G., a 20 year old woman, entered the hospital on May 4, 1946, with cardiac decompensation, due to insufficiency and stenosis of the mitral valve. She was dyspneic but not cyanotic. There was no jaundice. The liver was enlarged. There was massive edema of the legs. The blood count was as follows:

May 6, 1946 May 7, 1946

Nucleated red blood cells in congestive heart failure.

FRUMIN AM, MENDELL TH, MINTZ SS, NOVACK P, FAULK AT.

Circulation. 1959 Sep;20:367-70. No abstract available.

PMID: 13855805

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Nucleated Red Blood Cells in Congestive Heart Failure

By ABRAHAM M. FRUMIN, M.D., THEODORE H. MENDELL, M.D.,
SOLOMON S. MINTZ, M.D., PAUL NOVACK, M.D., AND ARTHUR T. FAULK, M.D.

NUCLEATED red cells may be discovered in the peripheral blood of patients with congestive heart failure. This phenomenon and its connotation of poor prognosis has not been generally recognized. Only a few reports, restricted primarily to the hematologic literature,¹⁻⁵ have stressed these findings. Because of the prognostic importance of peripheral nucleated red cells in congestive heart failure we are describing 5 cases with this finding (table 1) admitted to the Albert Einstein Medical Center, Southern Division, in a 6-year period. The previously reported cases are reviewed and analyzed.

REPORT OF CASES

Case 1. A 62-year-old white man, was admitted on December 2, 1951, with the chief complaint of cough, shortness of breath, and abdominal discom-

Case 2. A 63-year-old white woman, was admitted on March 3, 1952, because of edema of the legs and chest pain on effort. She was apparently well until 1949, when she experienced an episode of precordial pain associated with dyspnea, which subsequently increased and was followed by pedal edema. A questionable history of rheumatic fever in childhood was elicited.

Physical examination revealed cyanosis, dyspnea, and icterus. The blood pressure was 170/88. The heart was enlarged. A diastolic thrill was felt in the aortic area, and loud aortic and mitral systolic murmurs and a soft mitral diastolic murmur were heard. The liver was enlarged and there was pitting edema of the lower extremities. A diagnosis of rheumatic disease with mitral stenosis and insufficiency and aortic stenosis was made. X-rays of the chest revealed fluid in both pleural cavities and enlargement of all cardiac chambers. The electrocardiograph showed right heart strain. The patient became progressively more decompensated

- Çalışmanın ana hatları:
- 152 hasta (ICU: 7 gün-4-11 gün)
- ÇKKH prevalansı %54,6 (83/152)
- ICU mortalitesi % 49,4
- ÇKKH'nin varlığı ileri yaş, uzun süreli yoğun bakım, Yüksek hastalık skorları, sepsis ve non-koroner kardiyak etyoloji ile ilişkili bulunmuştur.

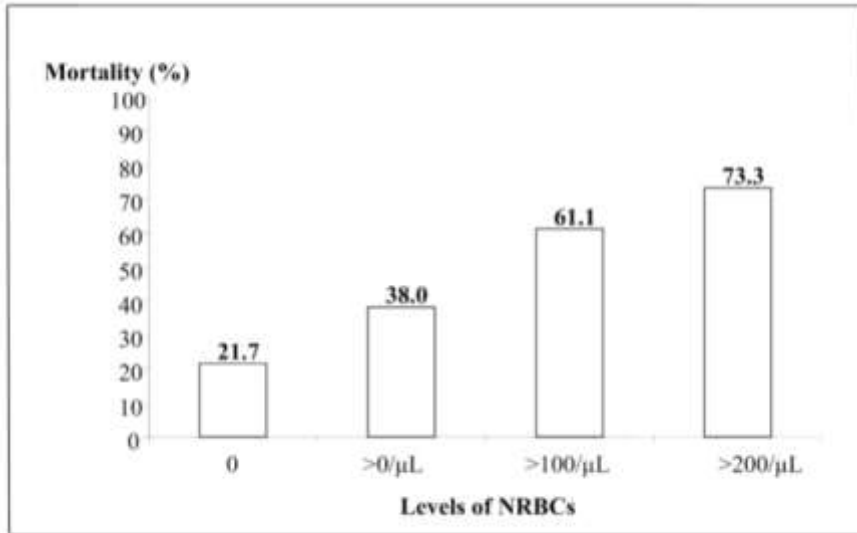
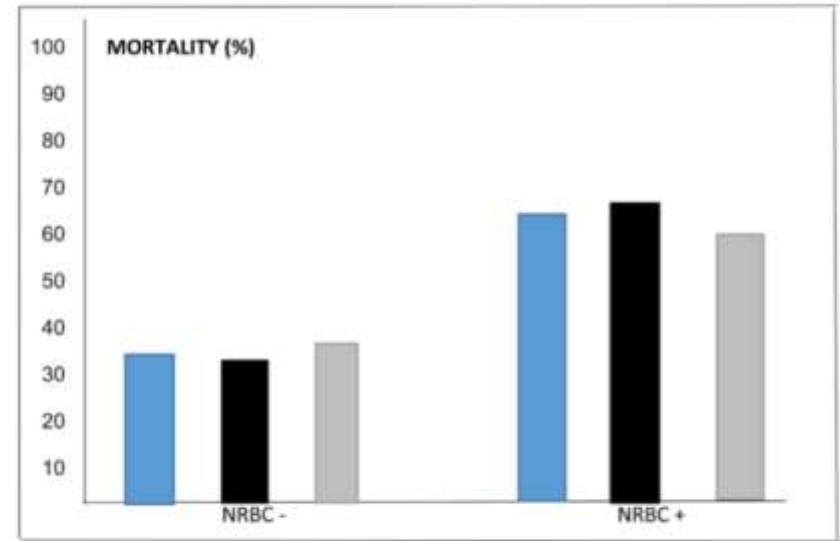


Fig 2. Mortality of ICU patients in relation to concentrations of nucleated red blood cells (NRBCs) P<0.001.



ALL PATIENTS:	NRBC - : 33.3% (23/69)	NRBC + : 64.45% (51/83)	P<0.001
CORONARY PATIENTS:	NRBC - : 32.5% (13/40)	NRBC + : 64.71% (22/34)	P=0.006
NON-CORONARY PATIENTS:	NRBC - : 34.5% (10/29)	NRBC + : 59.2% (29/49)	P=0.035

Fig 3. Mortality among coronary and non-coronary patients.

- Çalışmanın ana hatları:
- Yoğun bakım ünitesinde yüksek ÇKKH olan kişilerin mortalite oranı daha yüksek bulunmuştur.

Table 2. Distribution of the measure of the maximum NRBC during the hospital stay in the ICU.

NRBC	Statistics
Sample	152 patients
NRBC maximum rating	
Zero	69 (45.4%)
From 1 a 100	50 (32.9%)
From 101 a 200	18 (11.8%)
> 200	15 (9.9%)
Presence of NRBC per day of hospitalization	
1 ^o day	34/152* (22.4%)
2 ^o day	36/124 (29.0%)
3 ^o day	30/110 (27.3%)
4 ^o day	20/77 (25.9%)
5 ^o day	24/84 (28.6%)
6 ^o day	16/57 (28.1%)
7 ^o day	15/67 (22.4%)
8 ^o day	10/46 (21.7%)
9 ^o day	17/44 (38.6%)
After 9 ^o day	11/35 (31.4%)

* Number of patients with positive NRBC / Number of patients with measures NRBC.

doi:10.1371/journal.pone.0144259.t002

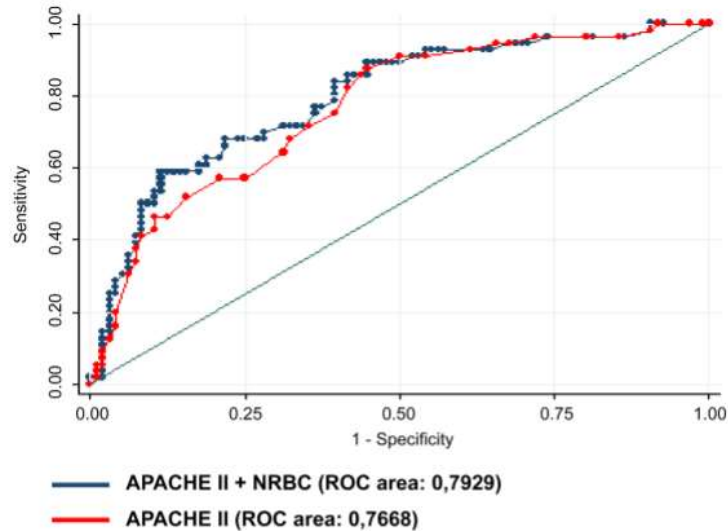


Fig 4. Comparison of ROC curves, $p = 0.01$.

Cerrahi Yoğun Bakım Hastalarında ÇKKH



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Clinica Chimica Acta 366 (2006) 329–335



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Daily monitoring of nucleated red blood cells in the blood of surgical intensive care patients

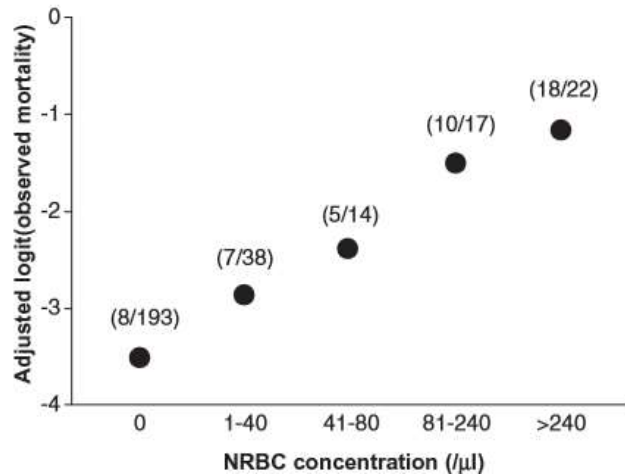
Axel Stachon ^{a,*}, Reiner Kempf ^a, Tim Holland-Letz ^b, Jochen Friesse ^c,
Andreas Becker ^a, Michael Krieg ^a

^a Institute of Clinical Chemistry, Transfusion and Laboratory Medicine, BG-University Hospital Bergmannsheil, Ruhr-University, Buerkle-de-la-Camp-Platz 1, D-44789 Bochum, Germany

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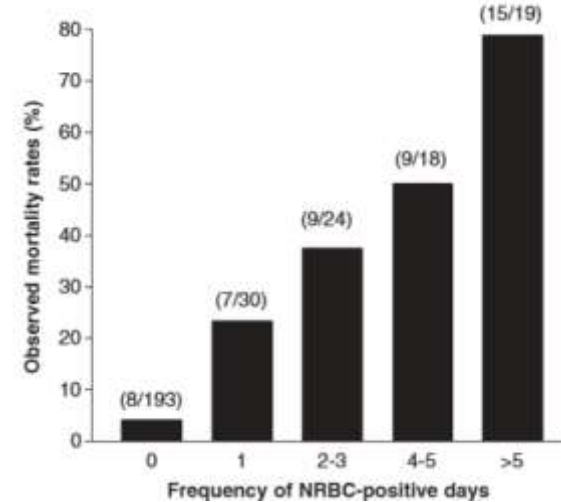
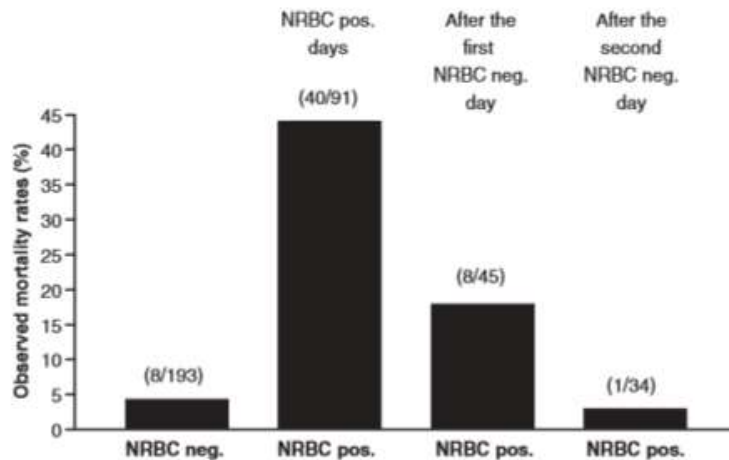
Received 20 October 2005; received in revised form 16 November 2005; accepted 16 November 2005



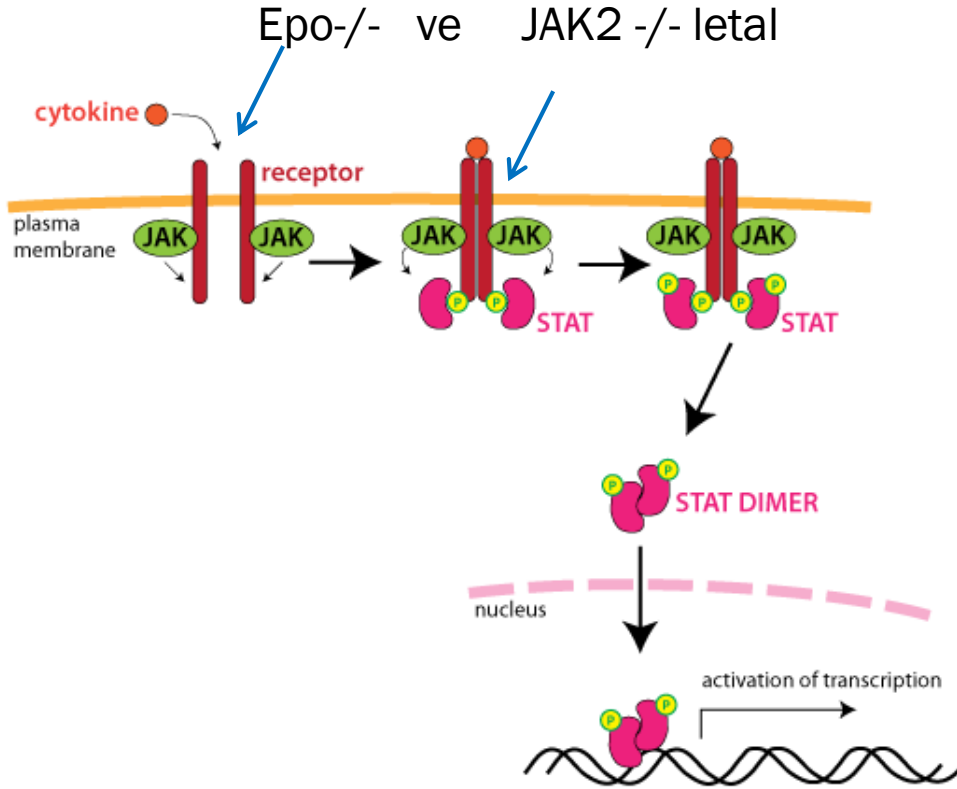
- Yoğun bakım ünitesinde cerrahi girişim geçiren 284 hastada yapılan bir çalışmada:
- Hasta ölümleri ile ÇKKH sayısı arasında doğrusal bir ilişki ortaya konmuştur.

Cerrahi Yoğun Bakım Hastalarında ÇKKH

- ÇKKH sayısı artışı mortalite ile ilişkili bulunmuştur.



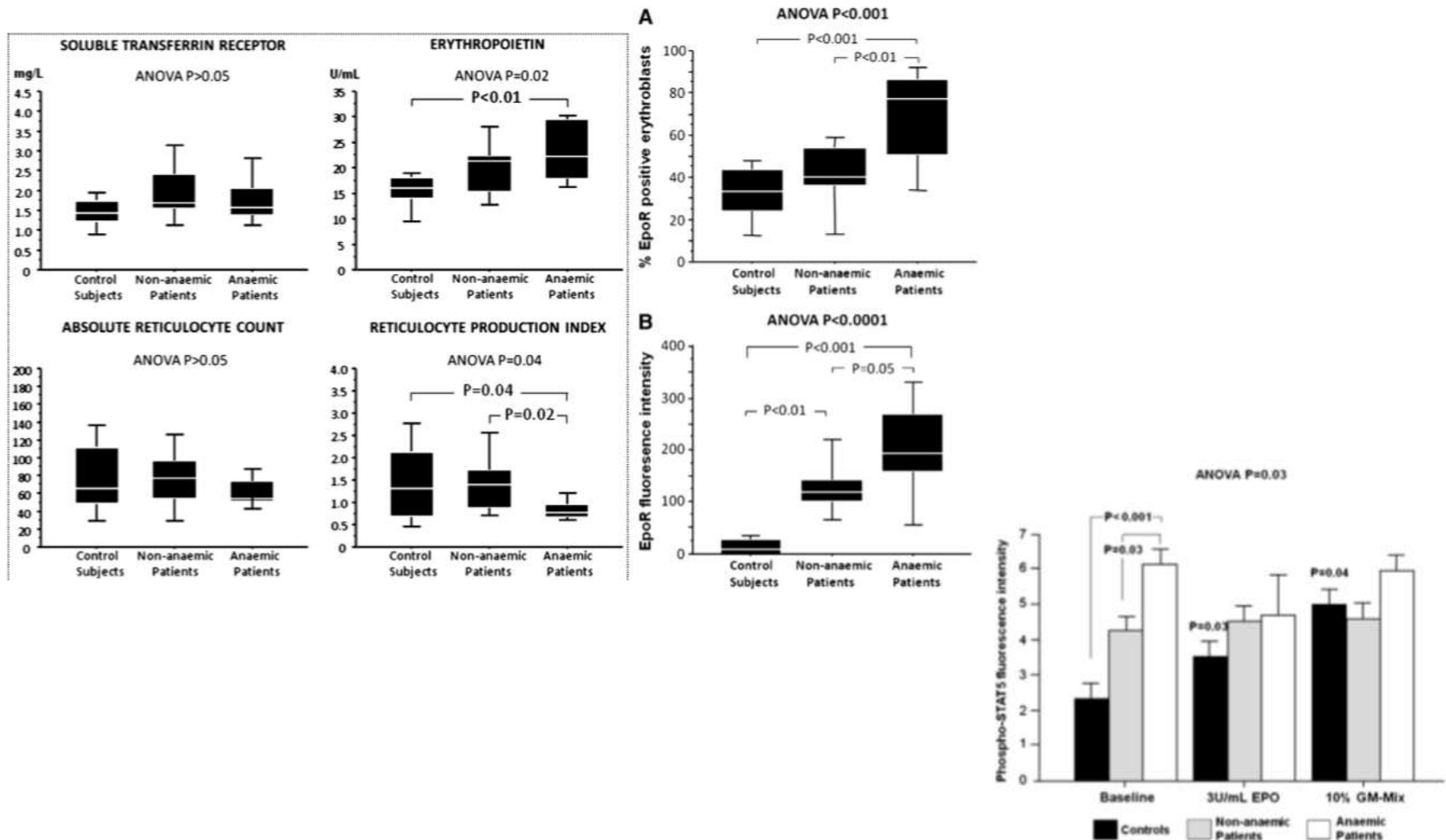
ÇKKH'nin-RBC'nin Oluşumu- Moleküler Mekanizmalar



- Epo , Epo R bağlanır
- *Janus Activated Kinase (JAK) ve Signal Transducer and Activator of Transcription (STAT)*
- Antiapoptotik genlerin transkripsiyonunu sağlar.

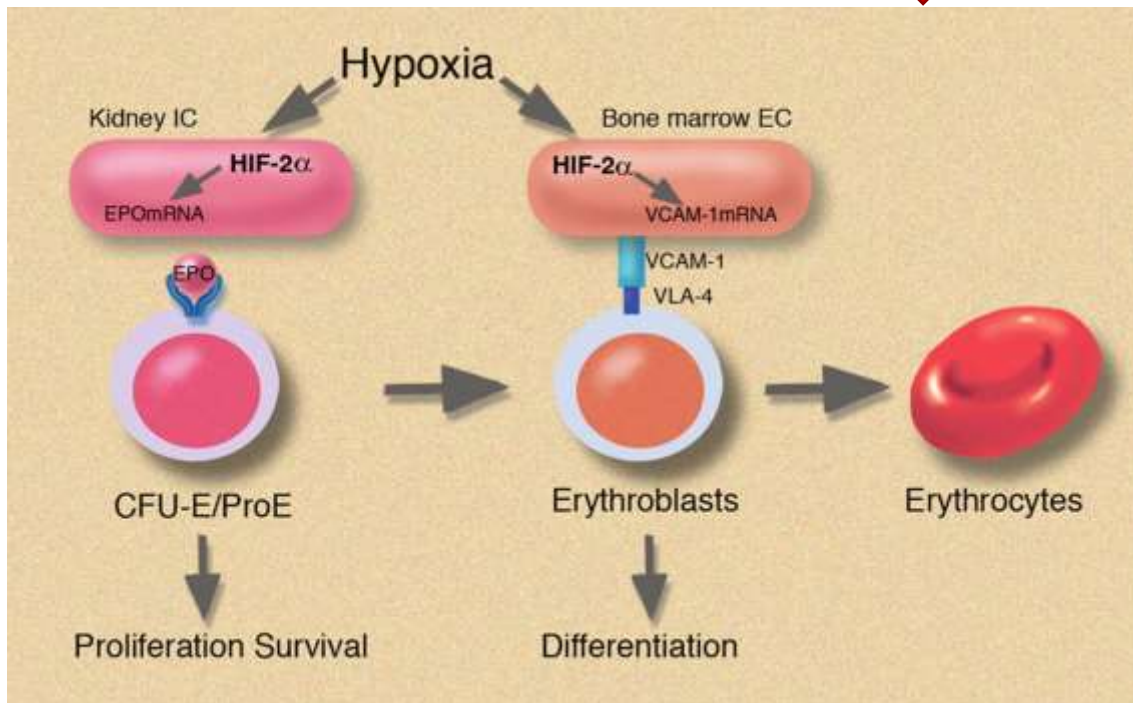
- Kronik kalp yetmezliği hastalarında EPO seviyeleri artmakta, ancak retikülosit sayısı anlamlı olarak azalmaktadır.

- Kronik kalp yetmezliği hastalarında anemi gelişimi ve JAK-STAT sinyal yolağı



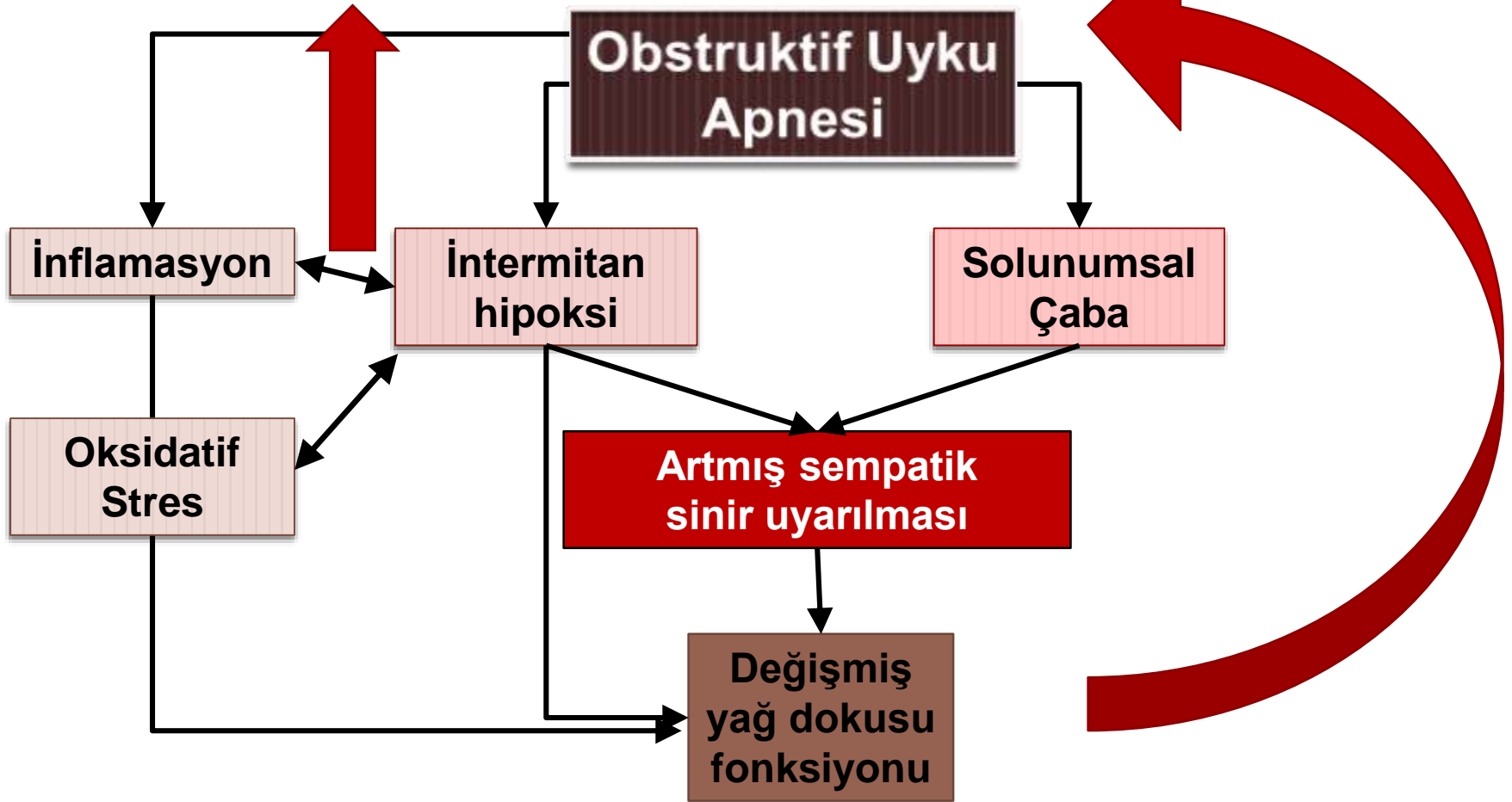
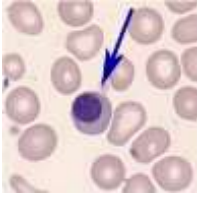
ÇKKH'nin-RBC'nin Oluşumu- Moleküler Mekanizmalar

İnflamasyon



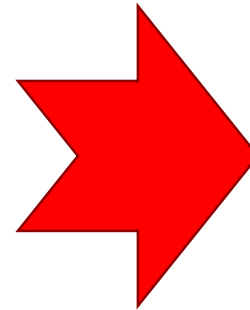


Hipotez...



Obstruktif Uyku Apne Sendromu (OUAS)

- OUAS uyku sırasında tekrarlayan üst solunum yolundaki daralmalar veya tıkanmalar nedeniyle soluk almada kesilmelerle kendini gösteren bir hastalıktır.
- Tekrarlayan soluk kesilmeleri uykunun devamlılığını bozar, derin ve dinlendirici bir uyku uyumasını engelleyerek, gündüzleri aşırı uykululuğa neden olur.
- Erişkinlerin 1/5- hafif; 1/15 orta derecede OUAS
 - Hipertansiyon % 83
 - Obezlerin % 77
 - Konjestif kalp yetmezliği %76
 - DM % 48



Patogenezi ???



Arginase activity and nitric oxide levels in patients with obstructive sleep apnea syndrome

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^IMarmara University, Vocational School of Health Services, Department of Medical Laboratory Techniques, Istanbul/Turkey. ^{II}Fatih Sultan Mehmet Research and Education Hospital, Chest Diseases Clinics, Istanbul/Turkey. ^{III}Gazikent Hasan Kalyoncu University, Vocational School of Health-related Professions, Gaziantep/Turkey. ^{IV}Trakya University, Faculty of Medicine, Department of Physiology, Edirne/Turkey.

Clinics (Sao Paulo) 69 (4): 247-252, 2014.

Sleep Breath (2008) 12:149–154
DOI 10.1007/s11325-007-0148-4

ORIGINAL ARTICLE

Circulating nitric oxide (NO), asymmetric dimethylarginine (ADMA), homocysteine, and oxidative status in obstructive sleep apnea–hypopnea syndrome (OSAHS)

**Yeşim Ozkan • Hikmet Fırat • Bolkan Şimşek •
Meral Torun • Sevgi Yardım-Akaydin**

Lipid peroxidation and osmotic fragility of red blood cells in sleep-apnea patients[☆]

Levent Öztürk^{a,*}, Banu Mansour^b, Meral Yüksel^c, A. Süha Yalçın^c,
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Received 5 February 2003; received in revised form 5 March 2003; accepted 6 March 2003

Abstract

Background: Obstructive sleep apnea (OSA) refers to the occurrence of episodes of complete or partial pharyngeal obstruction with oxyhemoglobin desaturation during sleep. These hypoxia/reoxygenation episodes may cause generation of reactive oxygen species. Reactive oxygen species are toxic to biomembranes and may lead to the peroxidation of lipids. We tested the hypothesis that obstructive sleep apnea is linked to increased oxidative stress and lipid peroxidation. In order to identify target tissue/cell damage, we studied the osmotic fragility of red blood cells. **Methods:** Six subjects polysomnographically diagnosed as obstructive sleep apnea syndrome and 10 controls were included. After all subjects gave written informed consent, blood samples were collected in the morning between 08:00 and 09:00 a.m. following polysomnography. Blood samples were immediately transferred to the laboratory. Glutathione, lipid peroxidation and osmotic fragility of red blood cells were measured manually. **Results:** Mean glutathione and lipid peroxidation concentrations of patients were not different than those of control subjects (105.6 ± 38.6 U/g Hb and 3.1 ± 2.3 nmol MDA/l vs. 100.6 ± 62.1 U/g Hb and 3.2 ± 2.8 nmol MDA/l, respectively). In both groups, osmotic fragility of red blood cells was not changed. **Conclusion:** The present study failed to support the hypothesis that obstructive sleep apnea is linked with increased oxidative stress and lipid peroxidation.

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Hipoksi

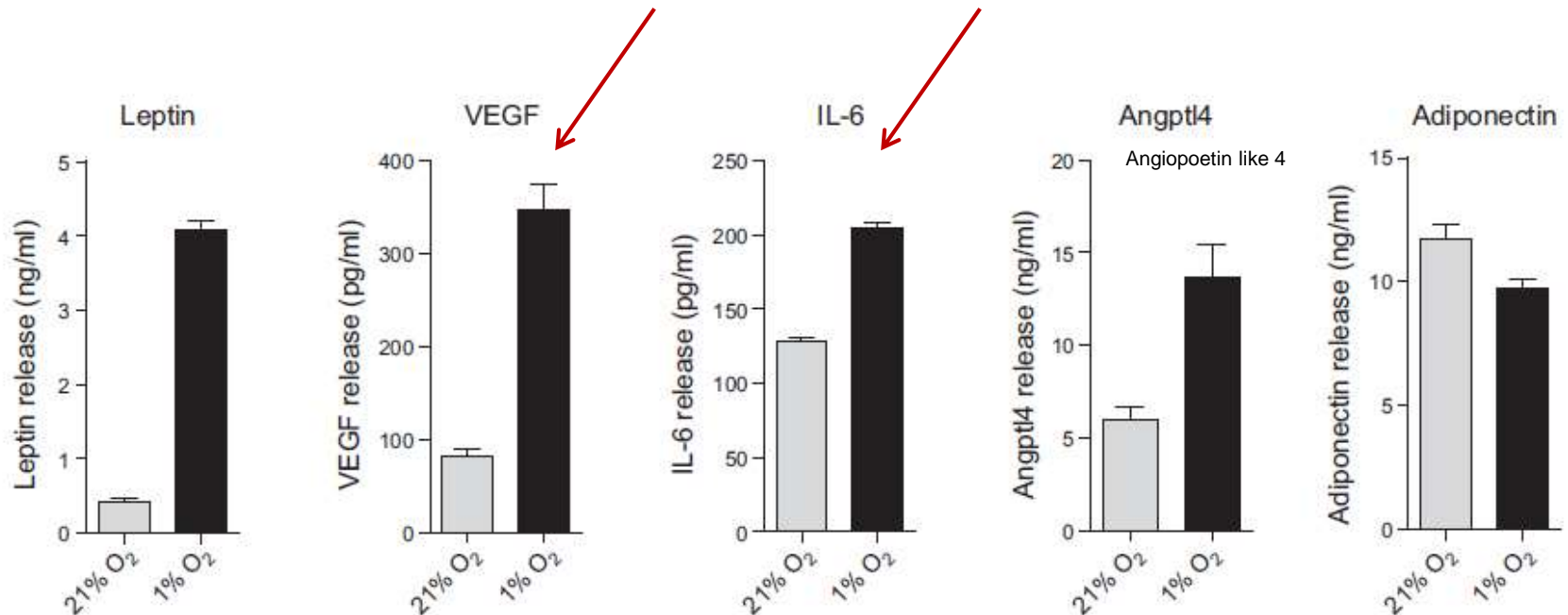


FIGURE 2. Example of the effects of hypoxia on the secretion of key adipokines by human adipocytes in cell culture. The data are derived from studies in which adipocytes were incubated in either 21% or 1% O₂ for 24 h (54, 188). The results are means \pm SE (bars; 6 observations per group), and for each adipokine, the difference between the hypoxic and control cells is statistically significant ($P < 0.01$ or better).

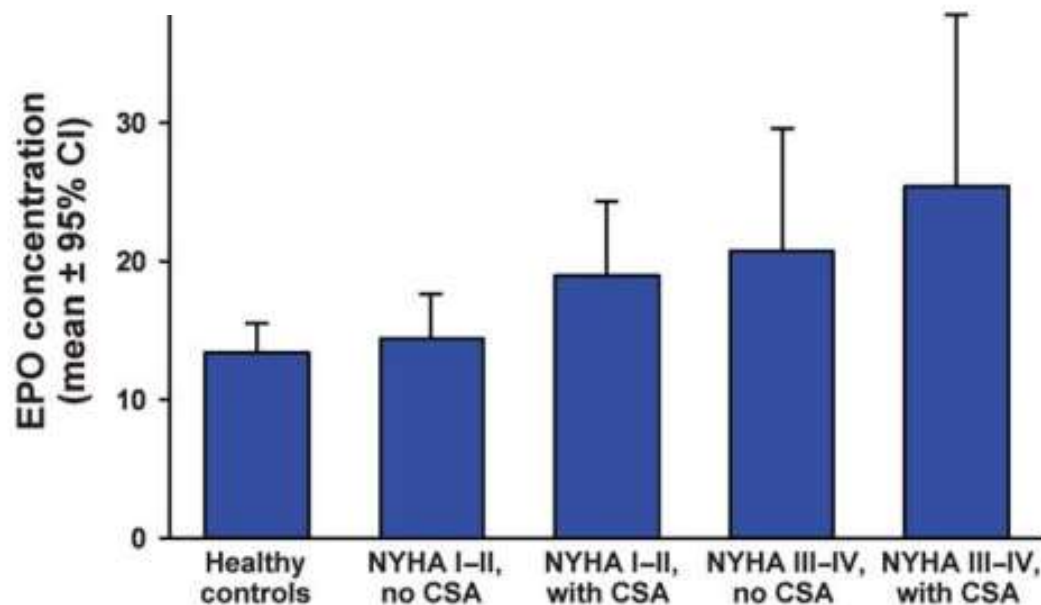
OUAS Eritropoetin Düzeyleri



European Journal of Heart Failure (2010) 12, 354–359
doi:10.1093/eurjhf/hfq005

Advanced heart failure and nocturnal hypoxaemia due to central sleep apnoea are associated with increased serum erythropoietin

Andrew D. Calvin¹, Virend K. Somers², David P. Steensma², Jose A. Rio Perez³, Christelle van der Walt², Jennifer M. Fitz-Gibbon², Christopher G. Scott², and Lyle J. Olson^{2*}



OUAS'da

- ÇÇKH artış gösterir mi?
- ÇÇKH + Kardiyovasküler hastalığı olan kişilerde artar mı?
- Eritropoetin düzeyi değişir mi?
- Orexin A ve/veya B düzeyleri ile ilişkisi?
- CPAP tedavisi alan kişilerde geri dönüş sağlayabilecek miyiz?
- ...

Sonuç

- Gelişen teknoloji ile birlikte, kan sayım cihazlarına eklenen ÇKKH parametresi ile
 - Yoğun bakım ünitesi hastaları
 - Kardiyovasküler-koroner
 - Yenidoğan
 - Hipoksi –inflamasyon
- İlişkisi olan hastalara yeni bir biyo-belirteç olarak kullanılabilecektir.





- Prof. Dr. Zerrin Pelin – Hasan Kalyoncu Ün. Sağlık Bil Fak. – Nöroloji
- Doç. Dr. Hacer Kuzu Okur- S.B. Fatih Sultan Mehmet Hastanesi -Göğüs Hast.
- Yard. Doç. Dr. Özlem Demirel - Bahçeşehir Ün. Tıp Fakültesi, -Biyokimya



Teşekkür Ederim...