

Glikokaliks Hasarının Klinik Belirteçleri

Dr. Halim Ulugöl

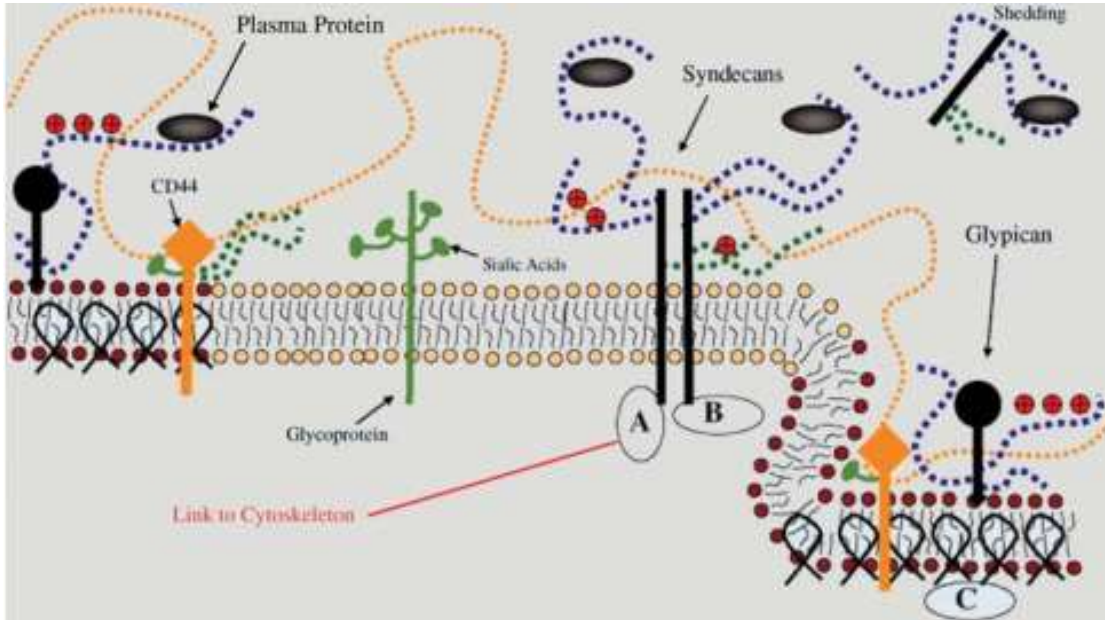
ACIBADEM ÜNİVERSİTESİ ANESTEZİYOLOJİ VE
REANİMASYON AD



Sunum Planı

- Glikokaliks komponentleri
- Glikokaliks ve KVC
- Glikokaliks ve DM
- Glikokaliks ve Sepsis
- Glikokaliksin Korunması ve Onarımı

Glikokaliks Komponentleri

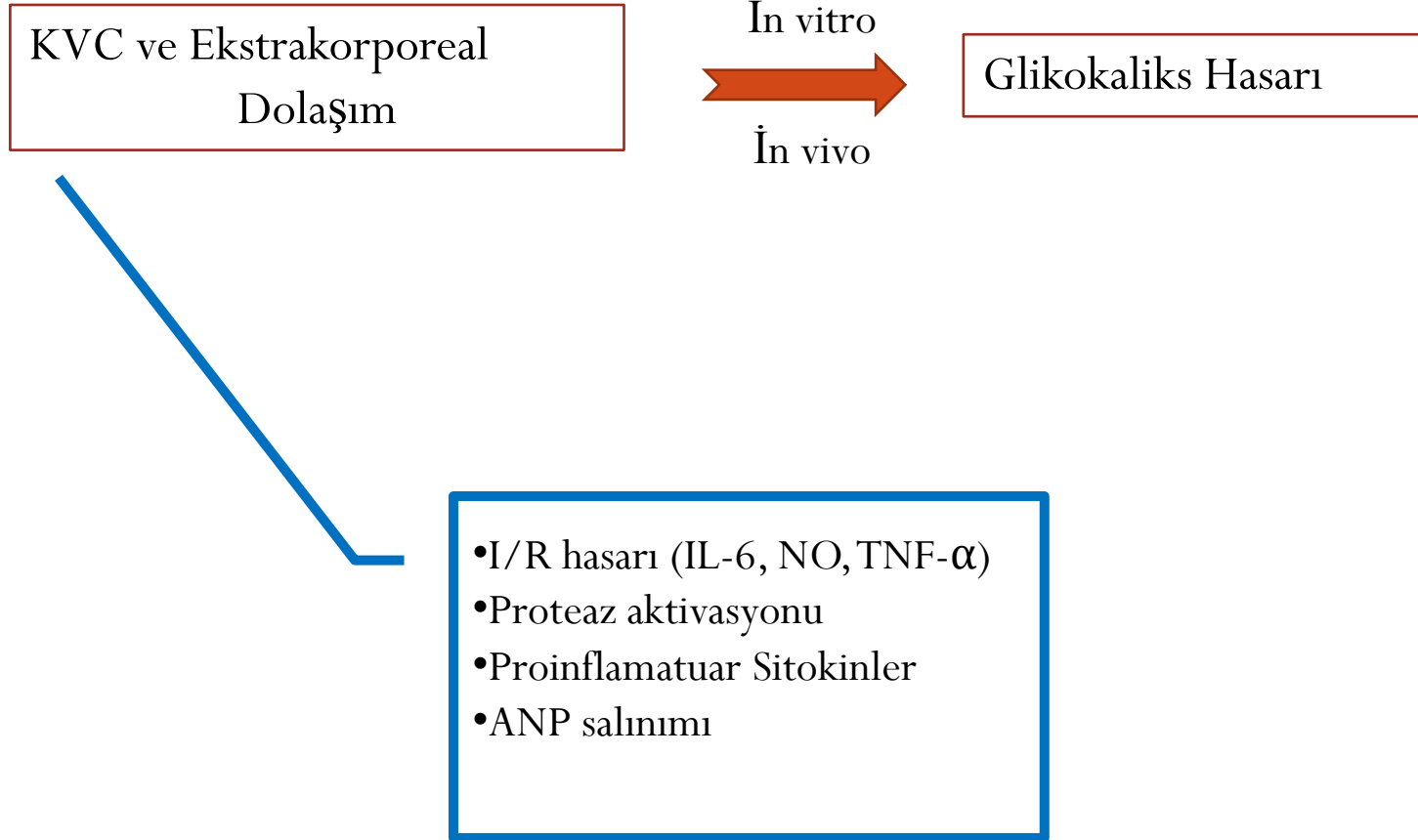


- Heparan Sülfat (GAG-%50)
- Kondroitin Sülfat (GAG)
- Dermatan Sülfat (GAG)
- Keratin Sülfat (GAG)
- Hyaluranik asit (GAG)
- Sialik Asit (Sialoproteinler)
- Syndecan-1 (Protein)
- Glypican (Protein)

The endothelial glycocalyx: a review of the vascular barrier.

Alphonsus CS, Rodseth RN. Anaesthesia. 2014 Jul;69(7):777-84. Apr 28.

Glikokaliks ve KVC



Shedding of the Endothelial Glycocalyx in Patients Undergoing Major Vascular Surgery With Global and Regional Ischemia

Markus Rehm, MD; Dirk Bruegger, MD; Frank Christ, MD; Peter Conzen, MD; Manfred Thiel, MD; Matthias Jacob, MD; Daniel Chappell, MD; Mechthild Stoeckelhuber, PhD; Ulrich Welsch, MD, PhD; Bruno Reichart, MD; Klaus Peter, MD; Bernhard F. Becker, MD, PhD

Circulation. 2007;116:1896-1906

- Grup-1: CPB + DHCA (n.12)
 - Grup-2: CPB (n:6)
 - Grup-3: Without CPB (n:14)
- Asendan aorta cerrahisi
- İnfrarenal aorta anevrizma

T0:İnd öncesi
T1: EKD başlangıcı
T2: EKD 5.dk
T3: EKD sonu
T4: Cerrahi sonu

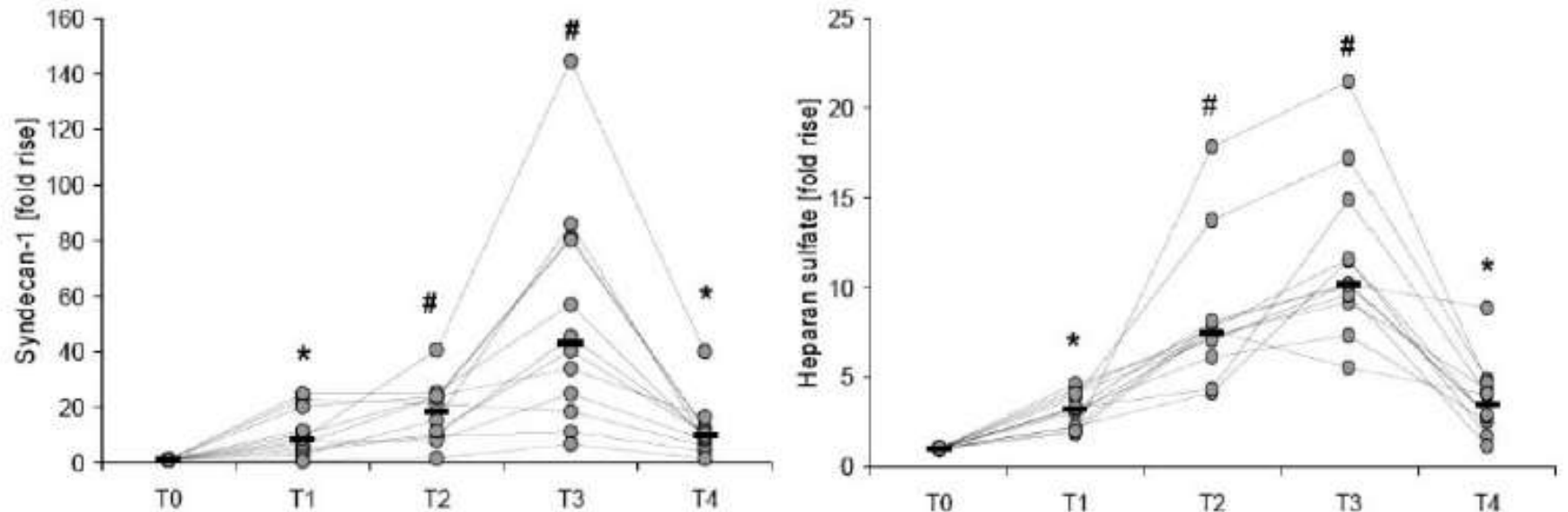
- Syndecan-1 ve Heparan Sülfat

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Circulation. 2007;116:1896-1906

A: DHCA



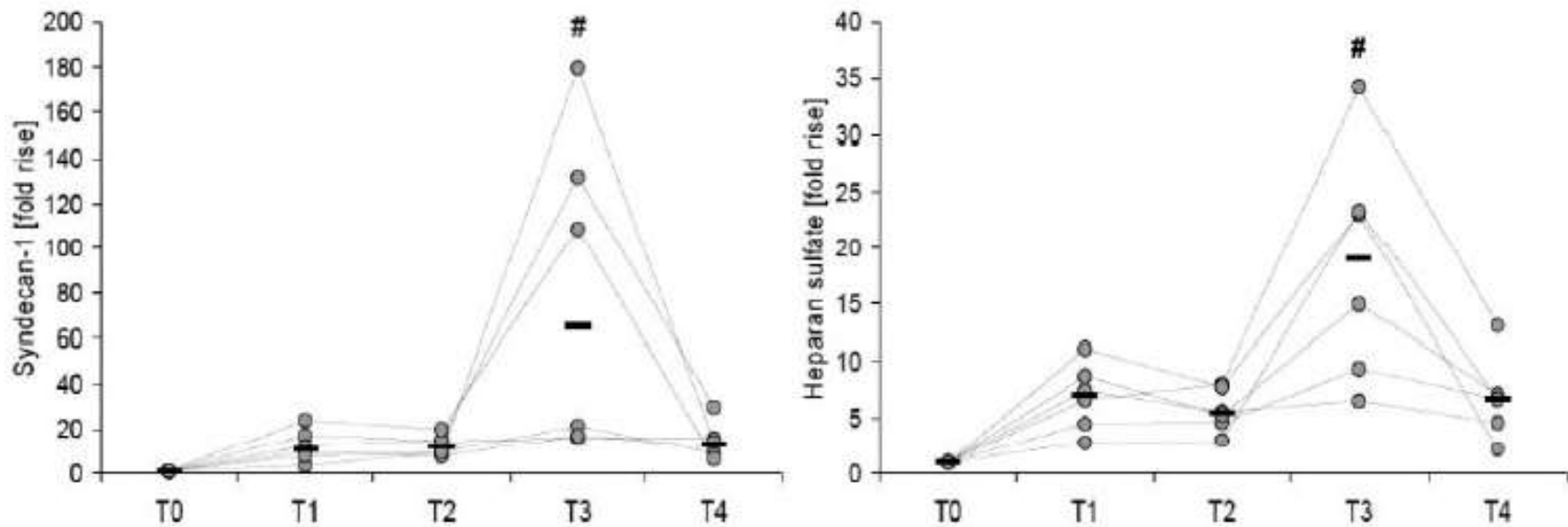
T0: İnd öncesi
T1: EKD başlangıcı
T2: EKD 5.dk
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Circulation. 2007;116:1896-1906

B: CBP



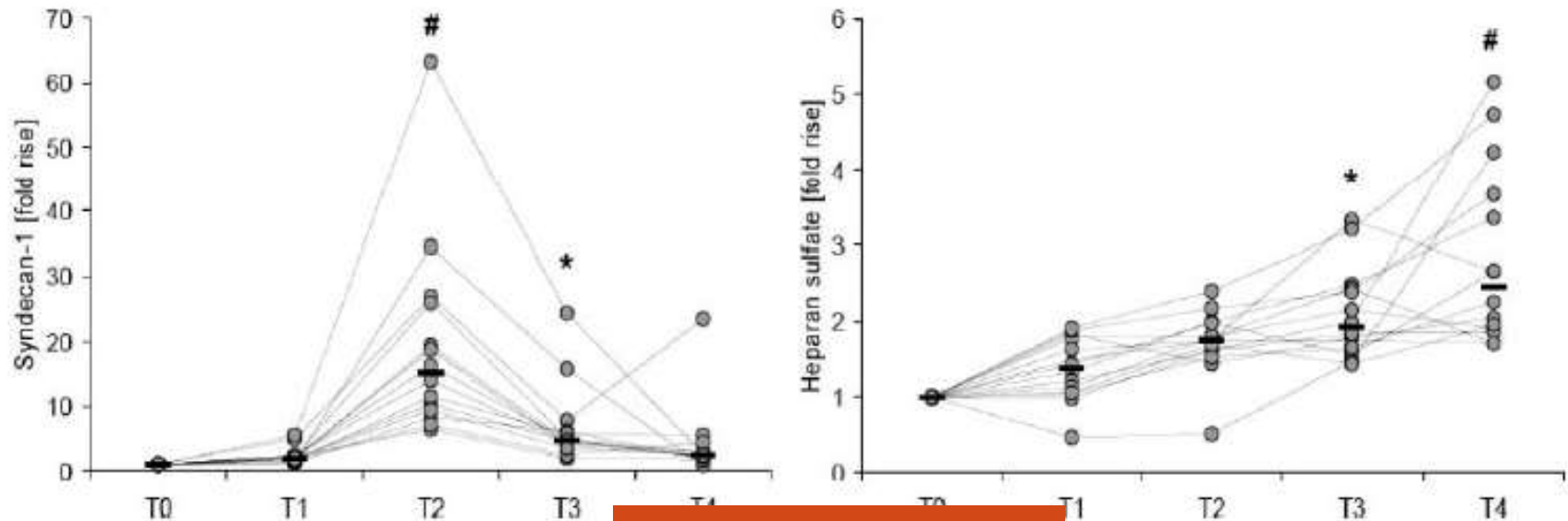
T0: İnd öncesi
T1: EKD başlangıcı
T2: EKD 5.dk
T3: EKD sonu
T4: Cerrahi sonu

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Circulation. 2007;116:1896-1906

C: AAA



T0: İnd öncesi
T1: A klempi 2. dk
T2: A klemp son 15.dk
T3: Cerrahi sonu
T4: Cer sonu 24.saat

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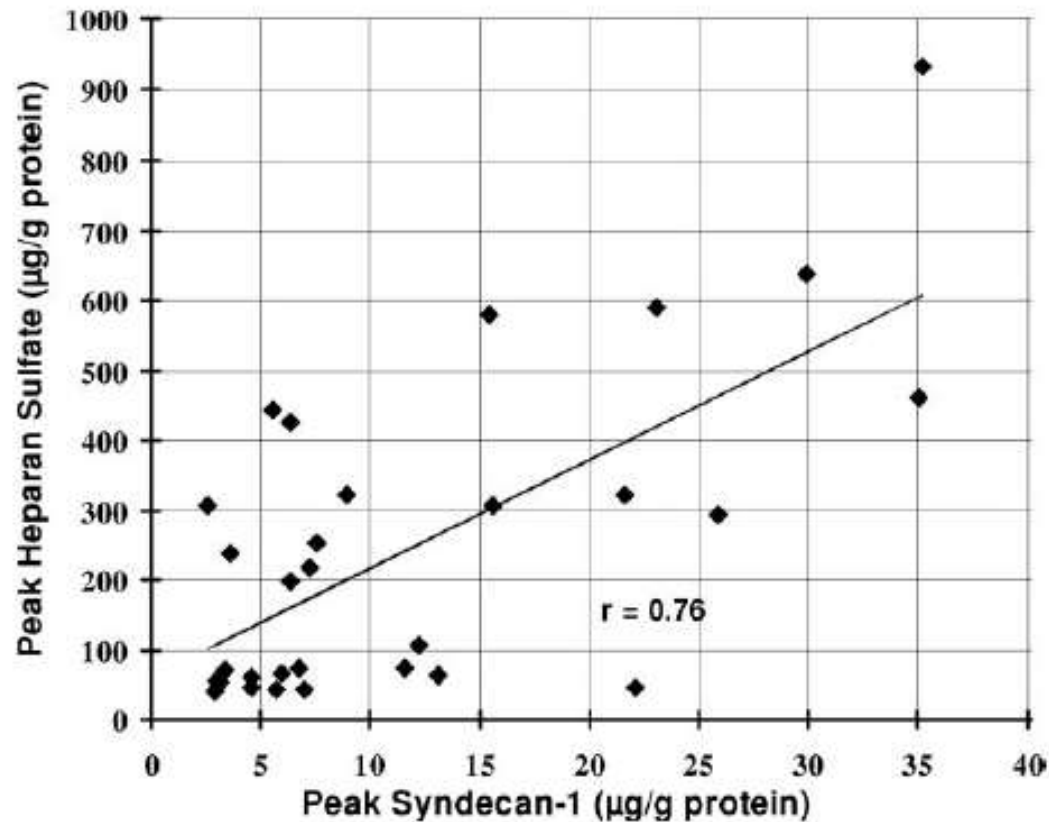
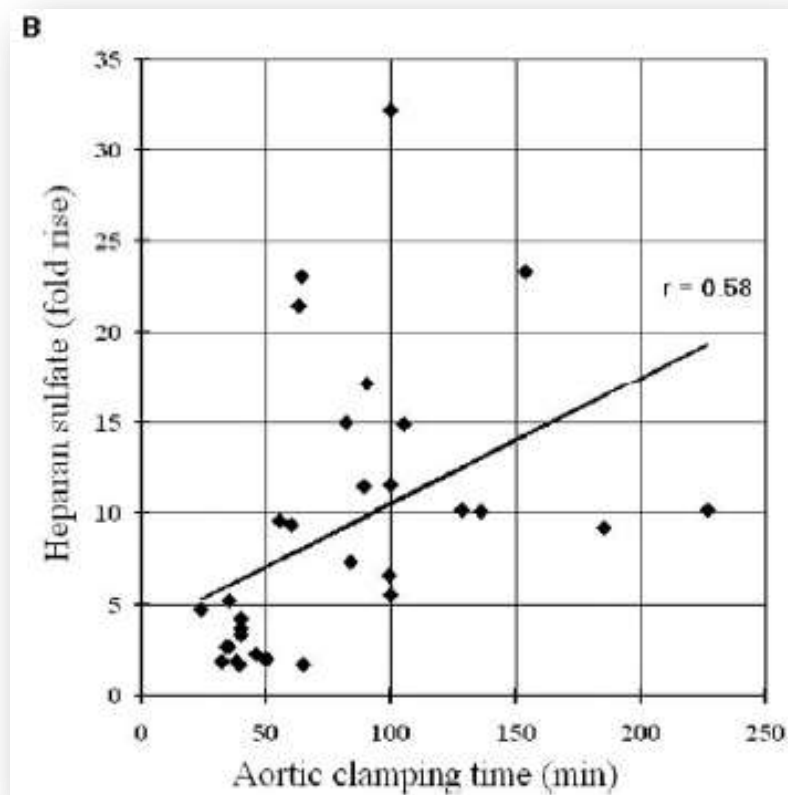
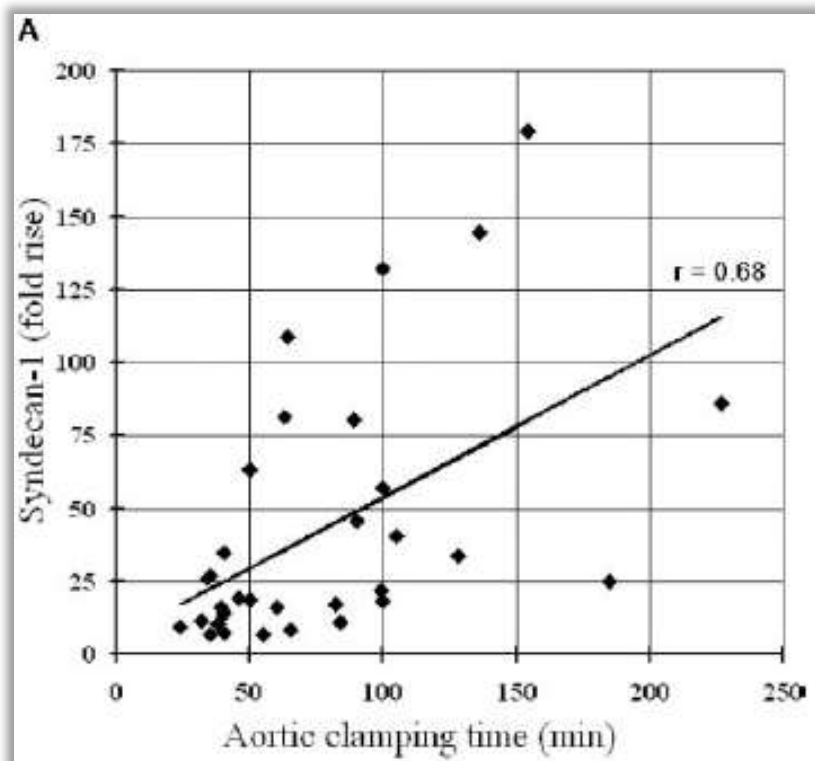


Figure 3. Correlation of plasma levels of heparan sulfate and syndecan-1 for individual patients in each group at time of postischemic reperfusion (DHCA group, T3; CPB group, T3; and AAA group, T2).

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Circulation. 2007;116:1896-1906



Shedding of the endothelial glycocalyx during cardiac surgery: On-pump versus off-pump coronary artery bypass graft surgery

Dirk Bruegger, MD,^{a,*} Markus Rehm, MD,^{a,*} Jan Abicht, MD,^a Joern Oliver Paul, MD,^a
Mechthild Stoeckelhuber, MD, PhD,^b Markus Pfirrmann, MSc,^c Bruno Reichart, MD,^d
Bernhard F. Becker, MD, PhD,^e and Frank Christ, MD,^a Munich, Germany

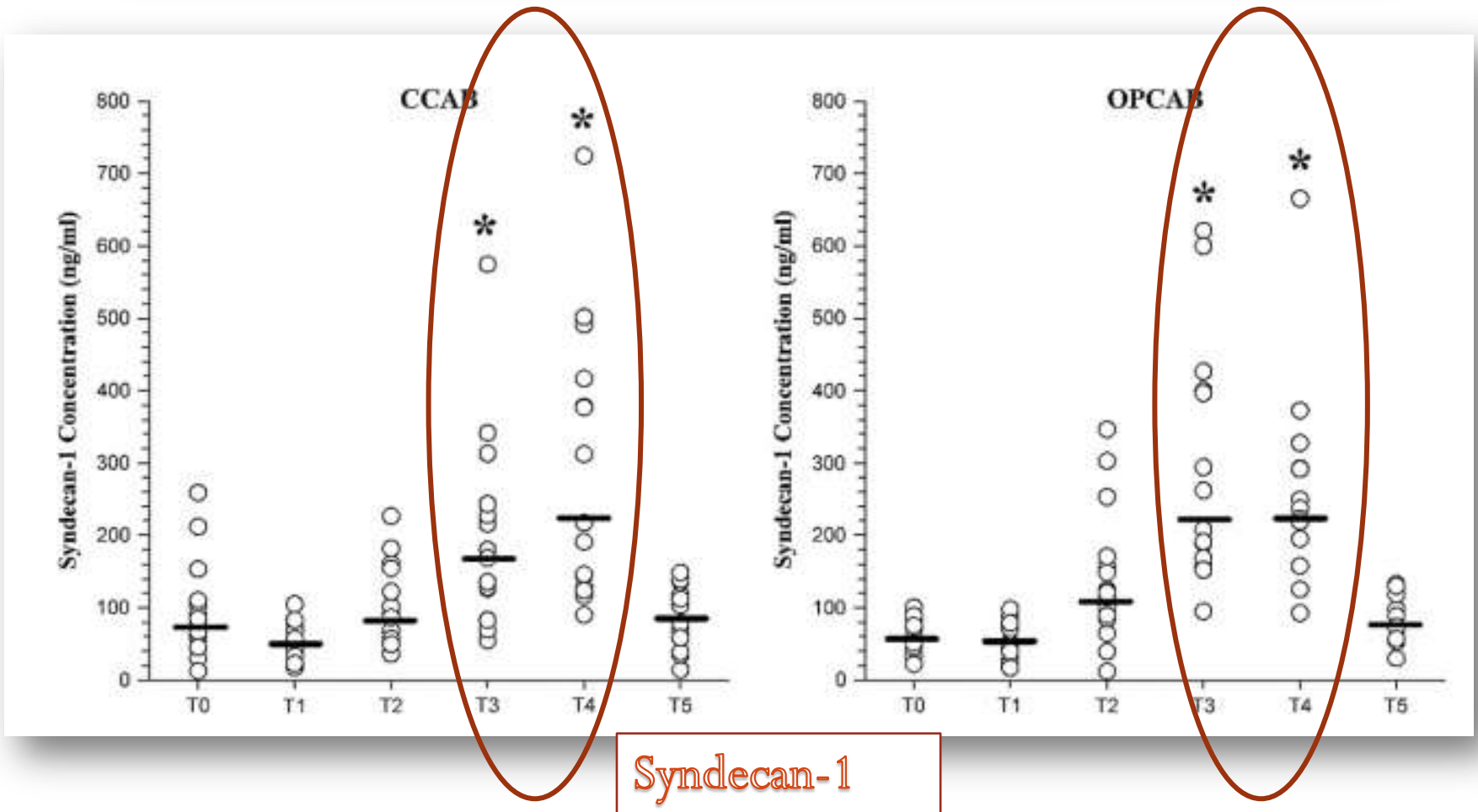
J Thorac Cardiovasc Surg 2009;138:1445-7

- Off-on pump
- T0, T1, T2, T3, T4 ve T5
- Syndecan-1 ve Heparan Sülfat

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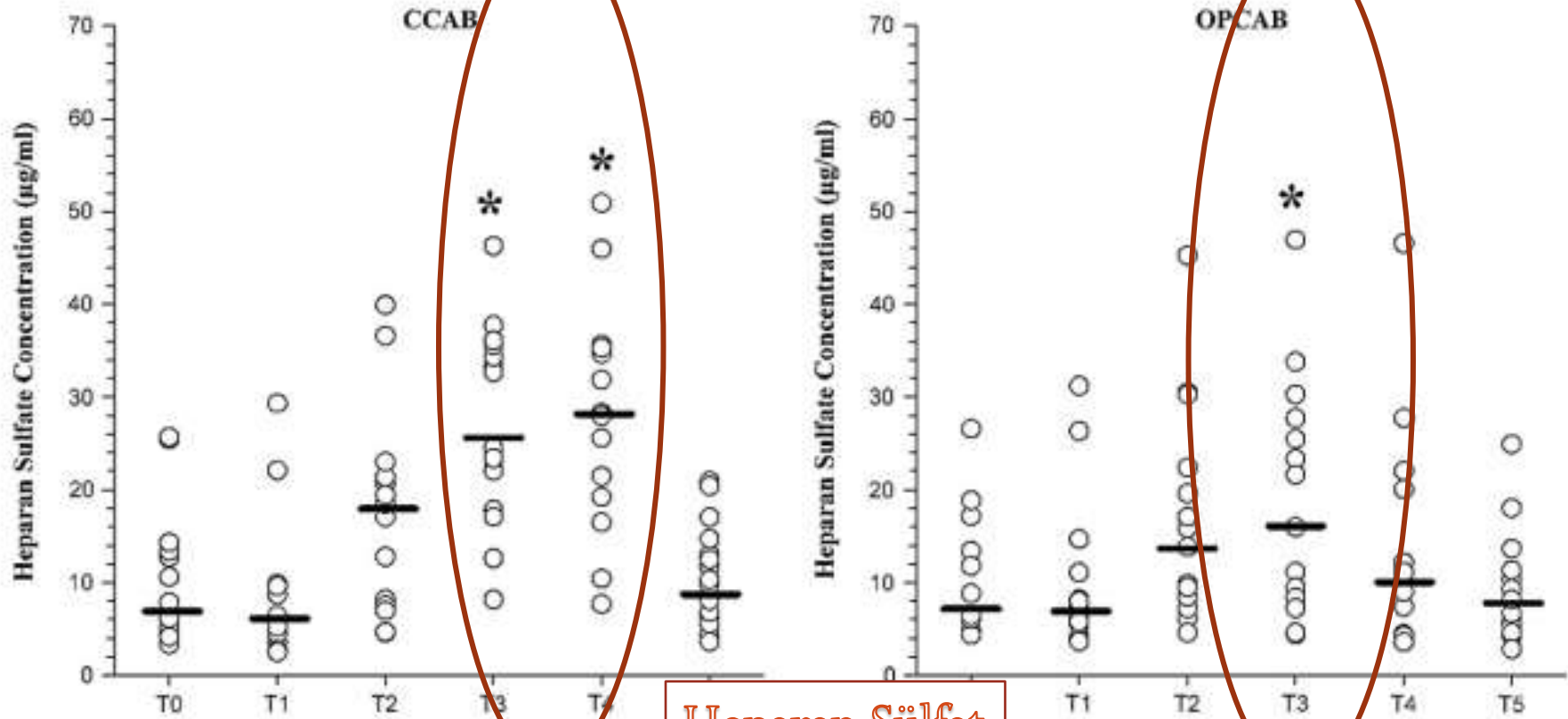
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J Thorac Cardiovasc Surg 2009;138:1445-7



Heparan Sulfat

Acute Degradation of the Endothelial Glycocalyx in Infants Undergoing Cardiac Surgical Procedures

Dirk Bruegger, MD,* Florian Brettner, MD,* Isabel Rossberg, Claudia Nussbaum, MD, Christian Kowalski, MD, Katarzyna Januszewska, MD, Bernhard F. Becker, MD, PhD, and Daniel Chappell, MD

Ann Thorac Surg 2015;99:926–31

- Grup-1: CPB
- Grup-2: CPB + AC
- Grup-3: CPB + AC + DHCA

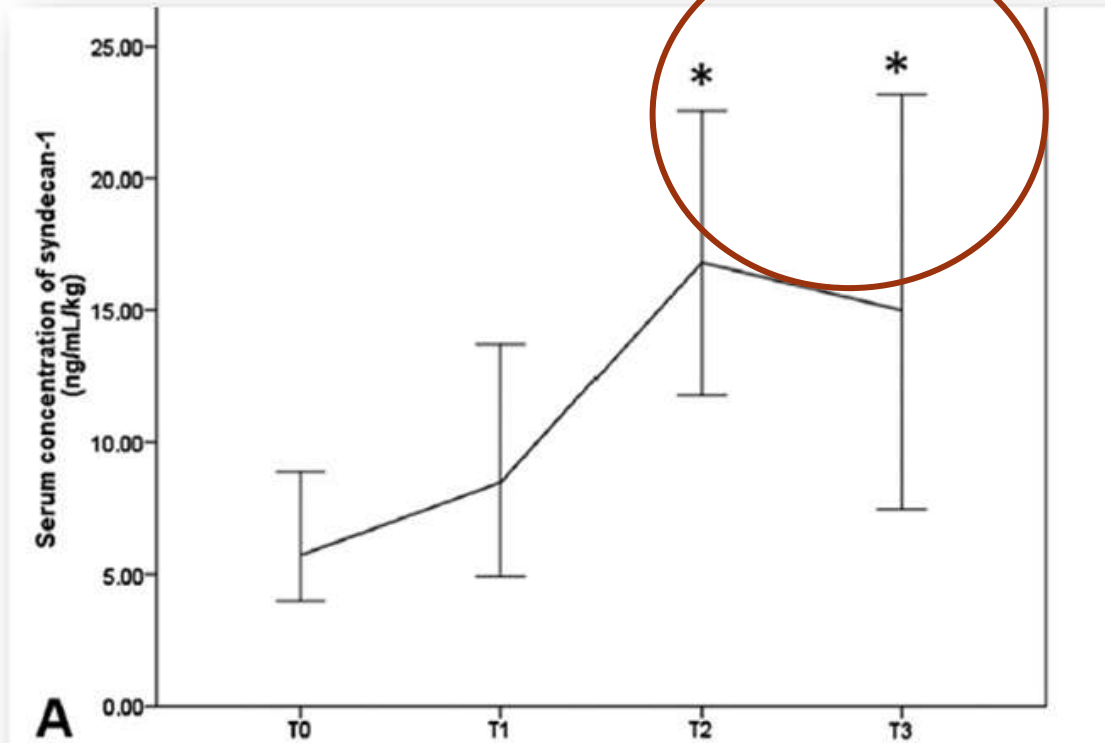
T0: İnd öncesi
T1: EKD öncesi
T2: EKD sonrası
T3: YBÜ kabul

- Syndecan-1 ve Hyaluronan

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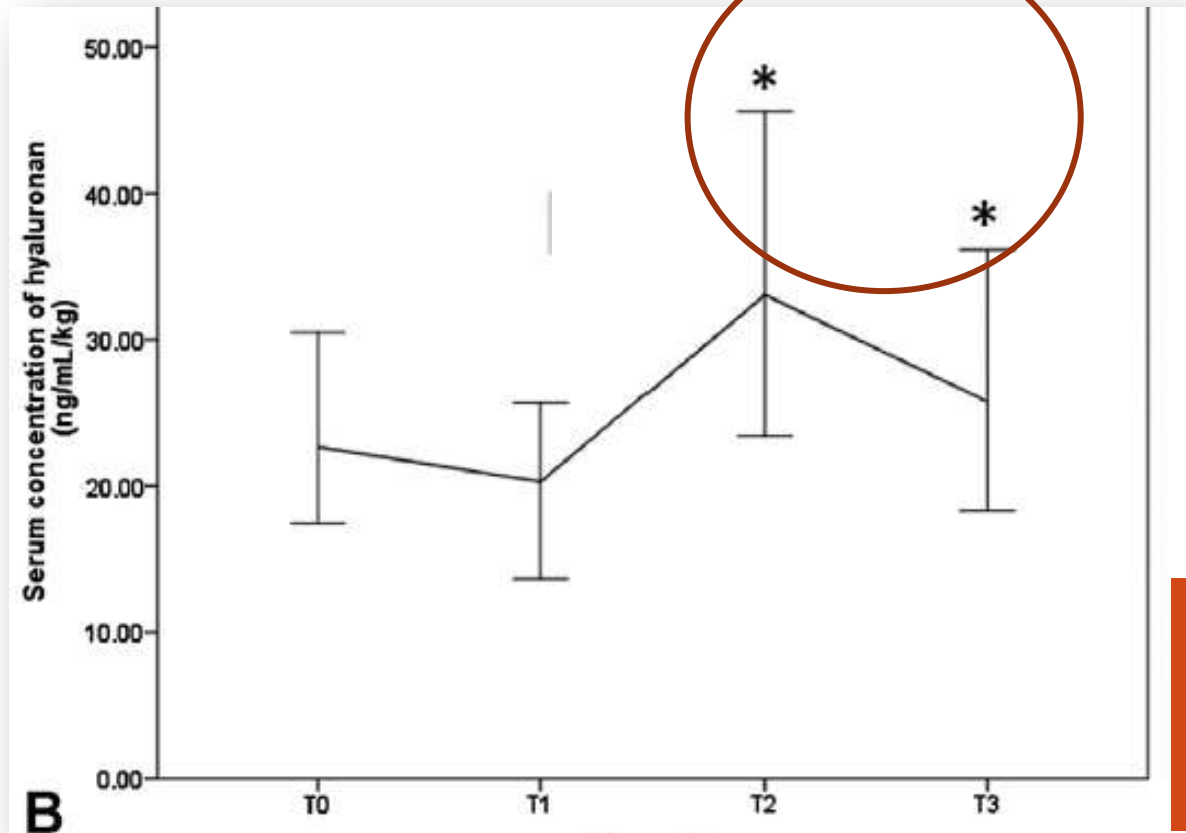
T0: İnd öncesi
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Syndecan-1

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Ann Thorac Surg 2015;99:926–31



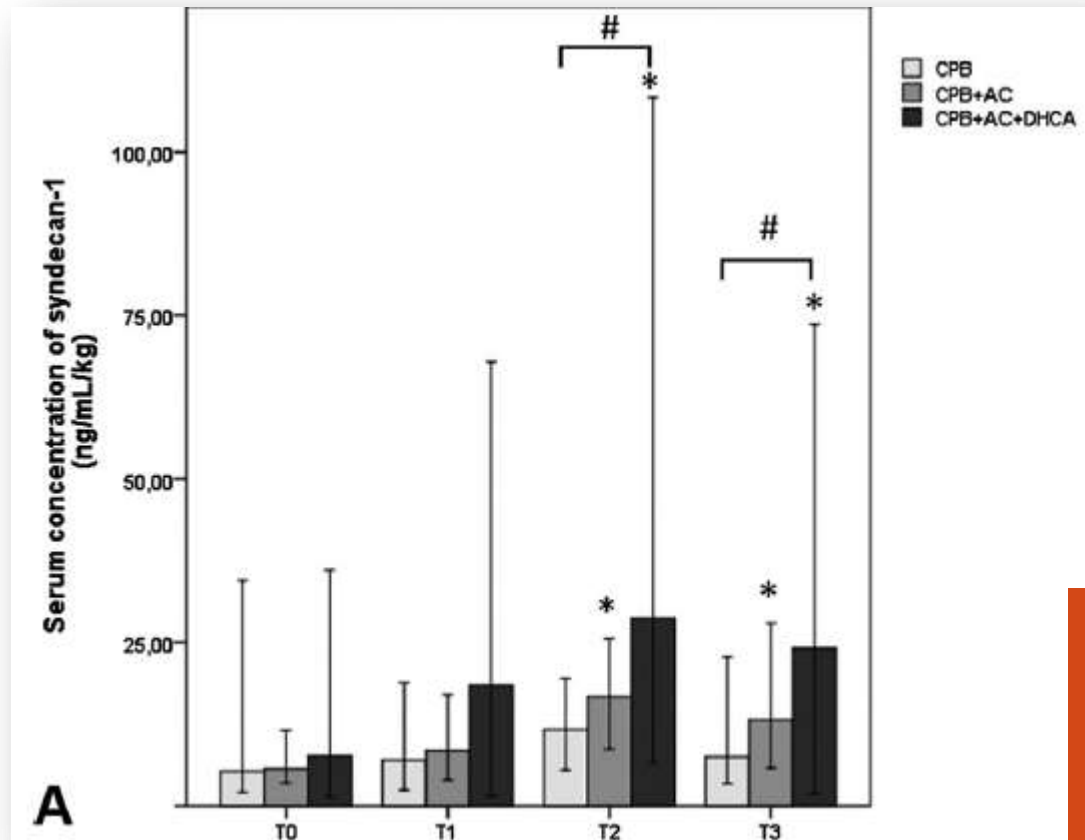
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Hyaluronan

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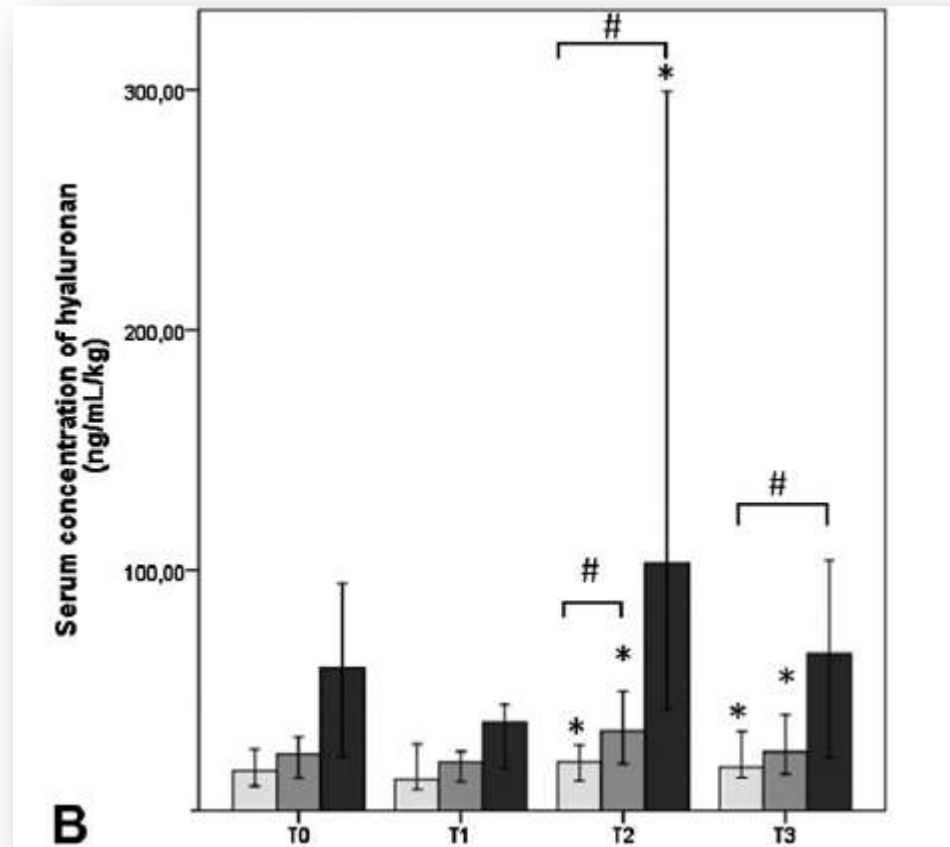
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Syndecan-1

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T0: İnd öncesi
T1: EKD öncesi
T2: EKD sonrası
T3: YBÜ kabul

Hyaluronan

Glikokaliks ve DM

- Uzun dönem DM hastalarında; Vasküler komplikasyonlar
 - Nefropati
 - Retinopati
 - Kardiyovasküler Hastalıklar
- Patogenez ? (Endotel Disfonksiyonu (en çok))

Khan F. Impaired skin microvascular function in children, adolescents, and young adults with type 1 diabetes. Diabetes Care 2000;23:215-20

Babar GS. Impaired endothelial function in preadolescent children with type 1 diabetes. Diabetes Care 2011;34:681-5.

Glikokaliks ve DM



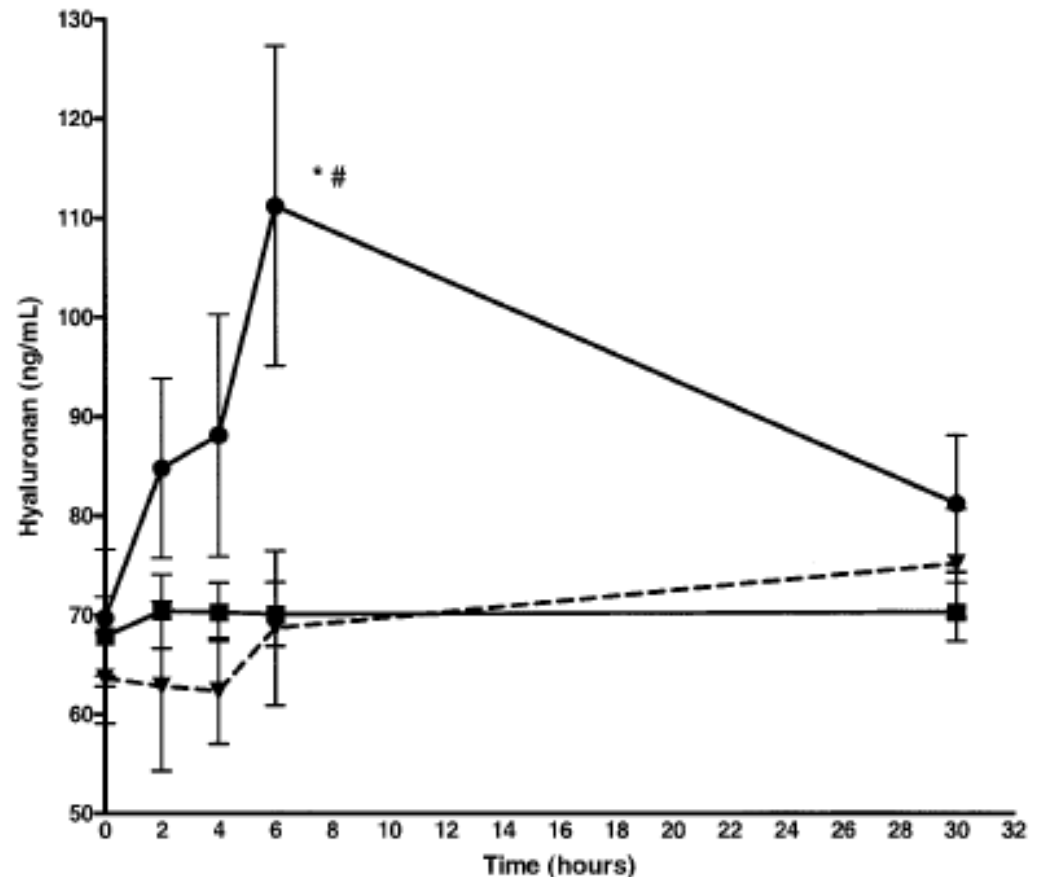
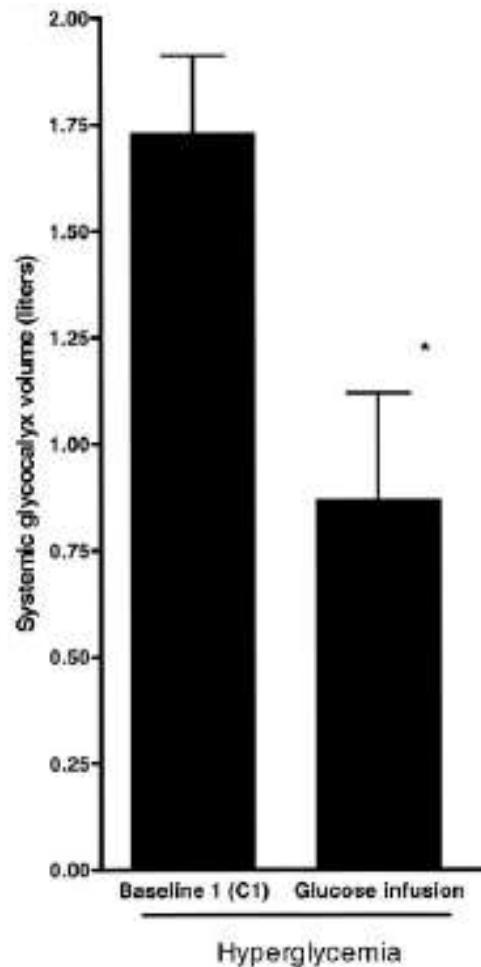
Brower JB, **High glucose** mediated loss of cell surface heparan sulfate proteoglycan impairs the endothelial shear stress response.

Cytoskeleton (Hoboken) 2010;67: 135-41

Loss of Endothelial Glycocalyx During Acute Hyperglycemia Coincides With Endothelial Dysfunction and Coagulation Activation In Vivo

Max Nieuwdorp,¹ Timon W. van Haften,² Mirella C.L.G. Gouverneur,³ Hans L. Mooij,¹ Miriam H.P. van Lieshout,¹ Marcel Levi,⁴ Joost C.M. Meijers,¹ Frits Holleman,⁴ Joost B.L. Hoekstra,⁴ Hans Vink,³ John J.P. Kastelein,¹ and Erik S.G. Stroes¹

Diabetes 55:480–486, 2006

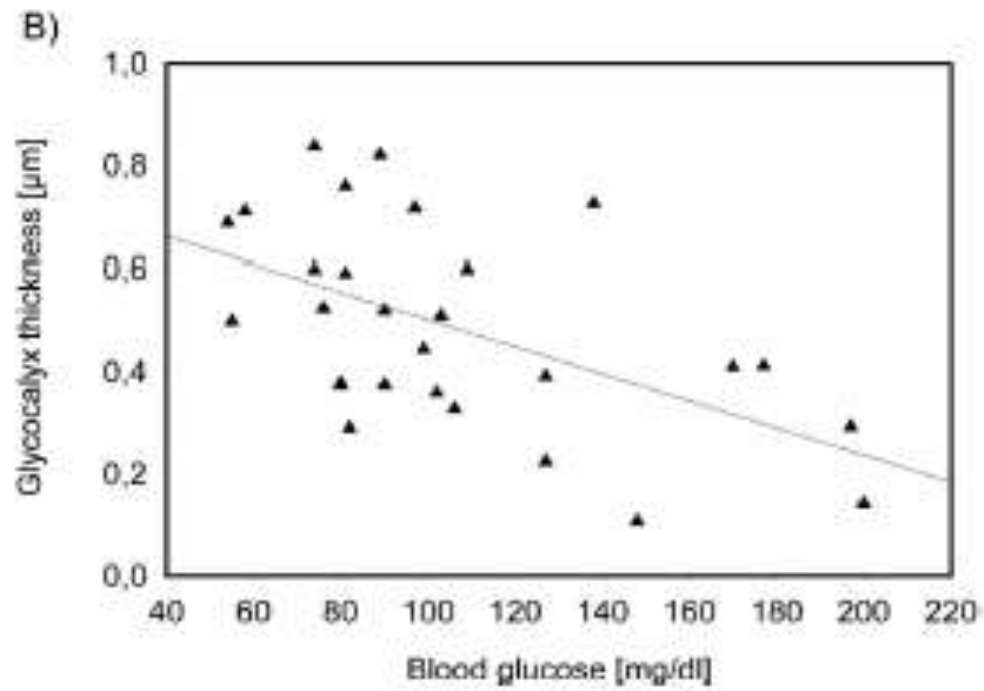
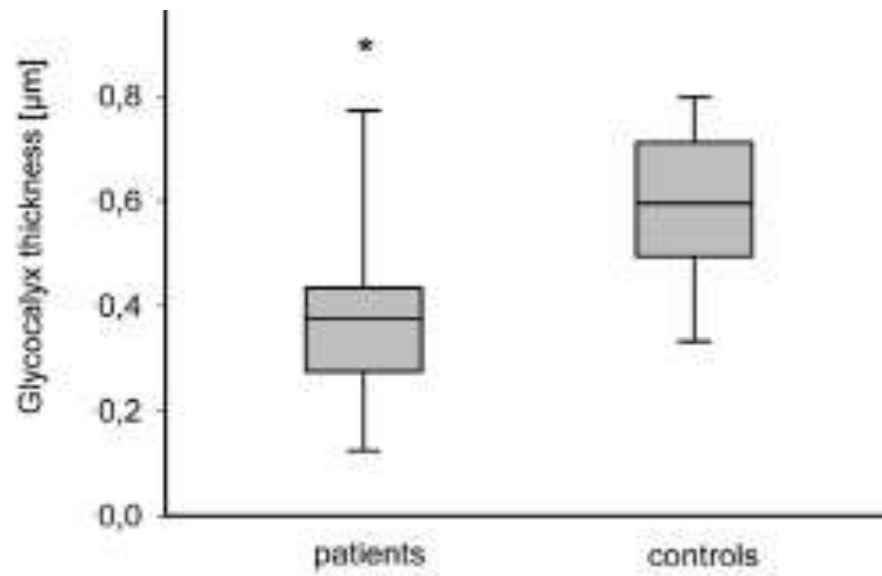


Early Microvascular Changes with Loss of the Glycocalyx in Children with Type 1 Diabetes

Claudia Nussbaum, MD¹, Ana Cavalcanti Fernandes Heringa, MD¹, Zuzana Mormanova, MD¹,
Alexandra F. Puchwein-Schwepcke, MD¹, Susanne Bechtold-Dalla Pozza, MD², and Orsolya Genzel-Boroviczény, MD¹

The Journal of Pediatrics 2014;164:584-9)

- Grup-1: Tip-I DM (9-13 Y 14 hasta)
- Grup-2 : Kontrol grubu (14 hasta)
- SDF Microvascular Imaging (sublingual)
 - TVD (Total vessel density)
 - MFI (Mean flow index)
 - Glikokaliks kalınlığı

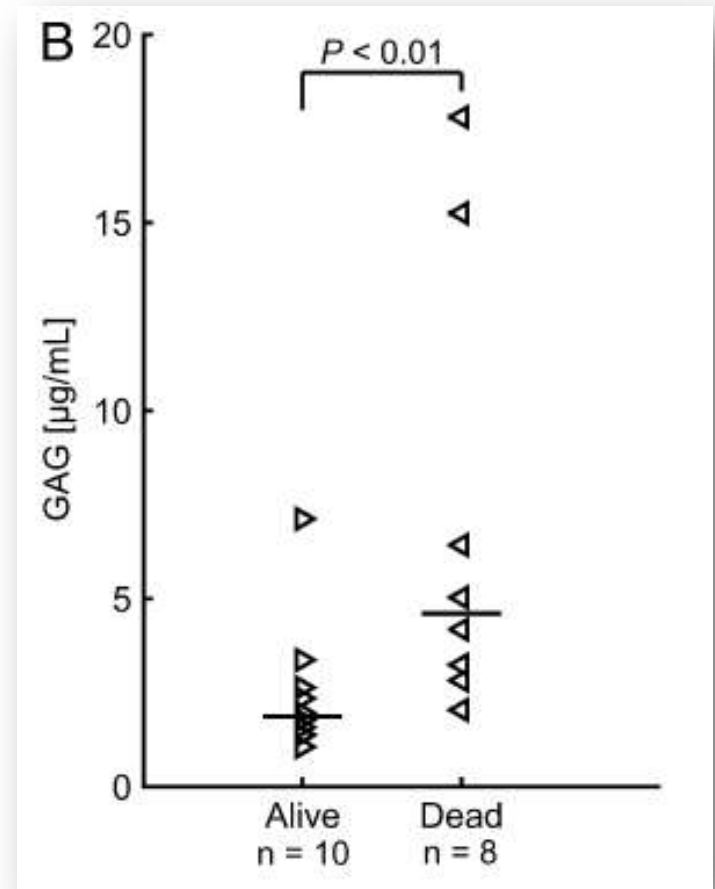
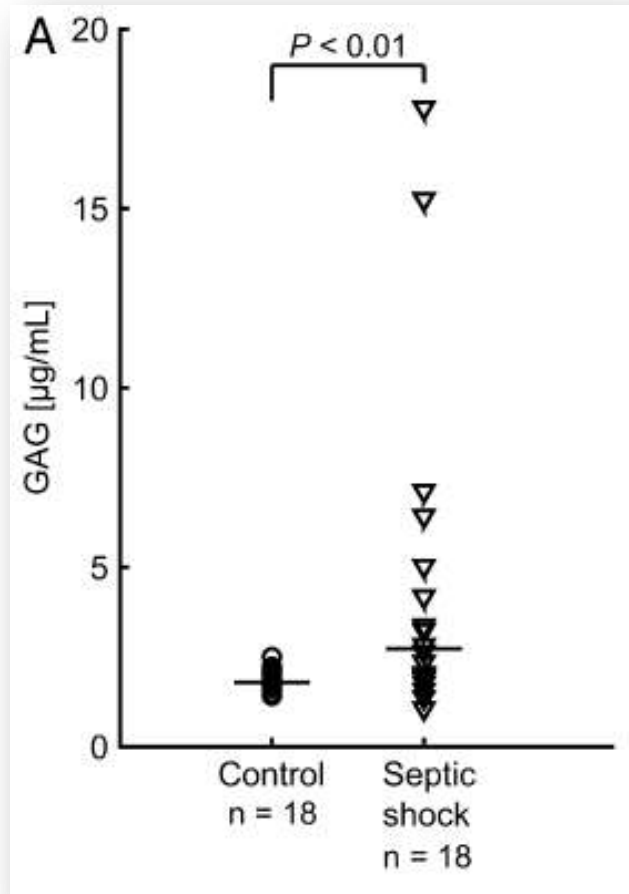


Glikokaliks ve Sepsis

- Glikokaliks hasar markırlarında artış
(Syndecan-1,heparan sülfat, hyaluronik asit...)
- Glikokaliksi korumada veya tedavide hedef ?

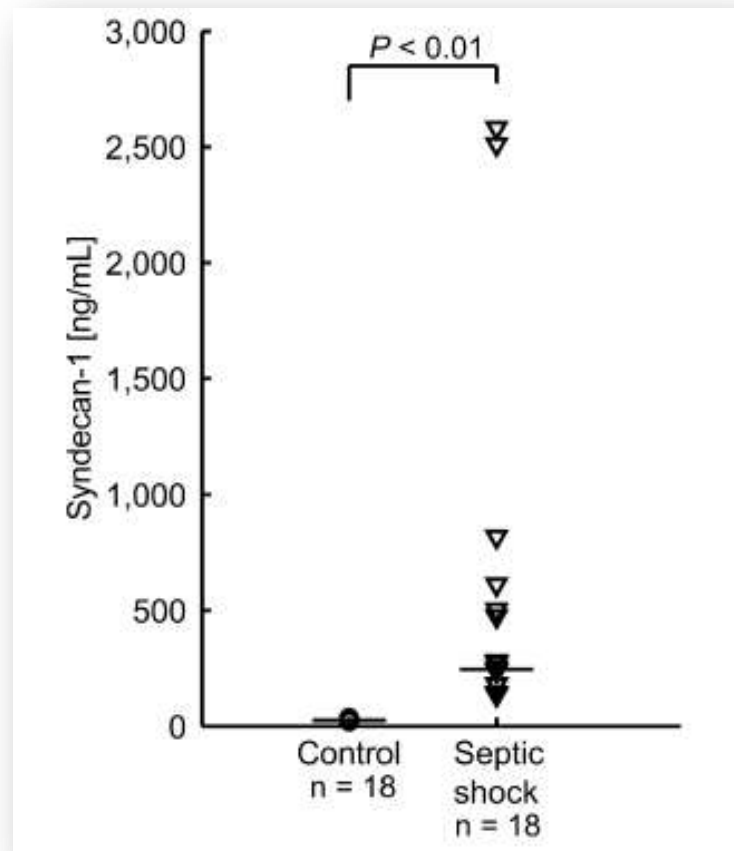
Increased levels of glycosaminoglycans during septic shock: relation to mortality and the antibacterial actions of plasma

Shock. 2008 Dec;30(6):623-7



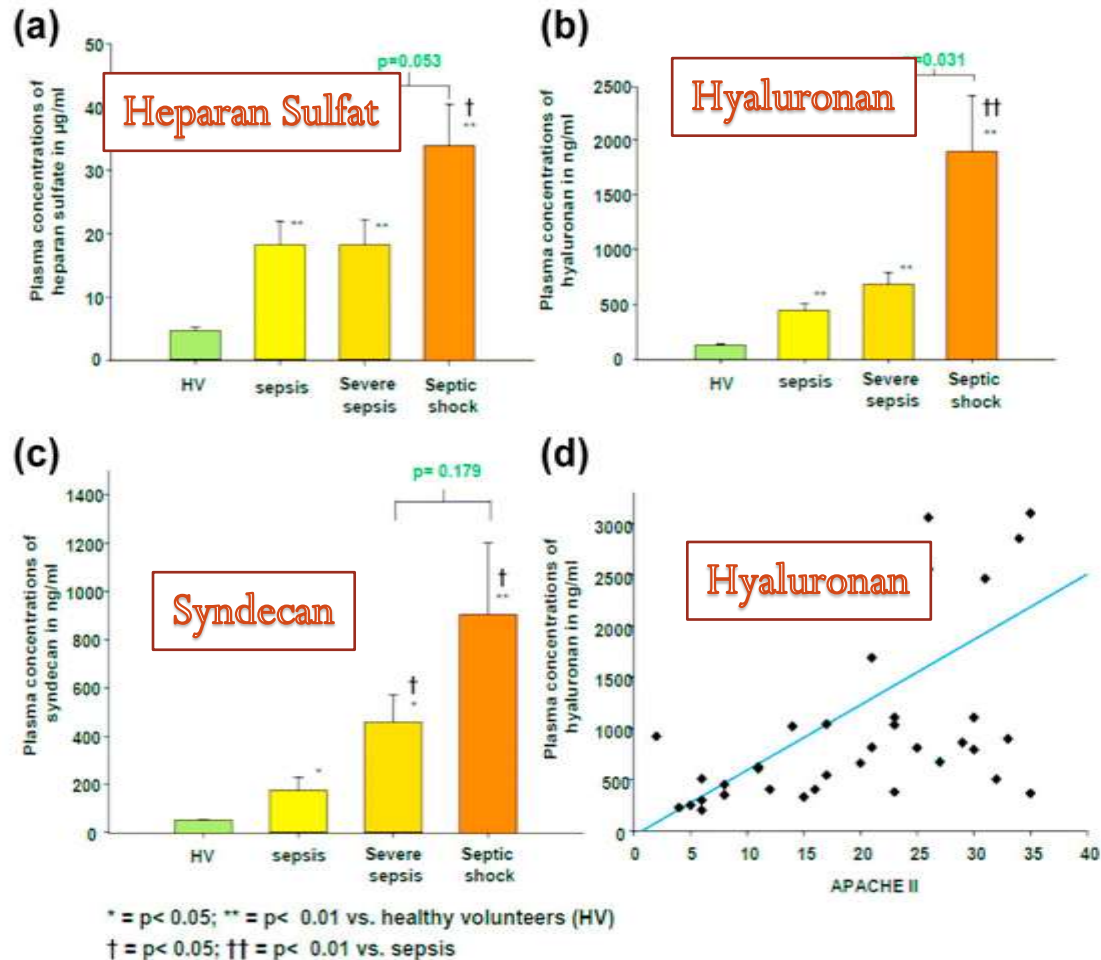
Increased levels of glycosaminoglycans during septic shock: relation to mortality and the antibacterial actions of plasma

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The Endothelial Glycocalyx Degenerates With Increasing Sepsis Severity

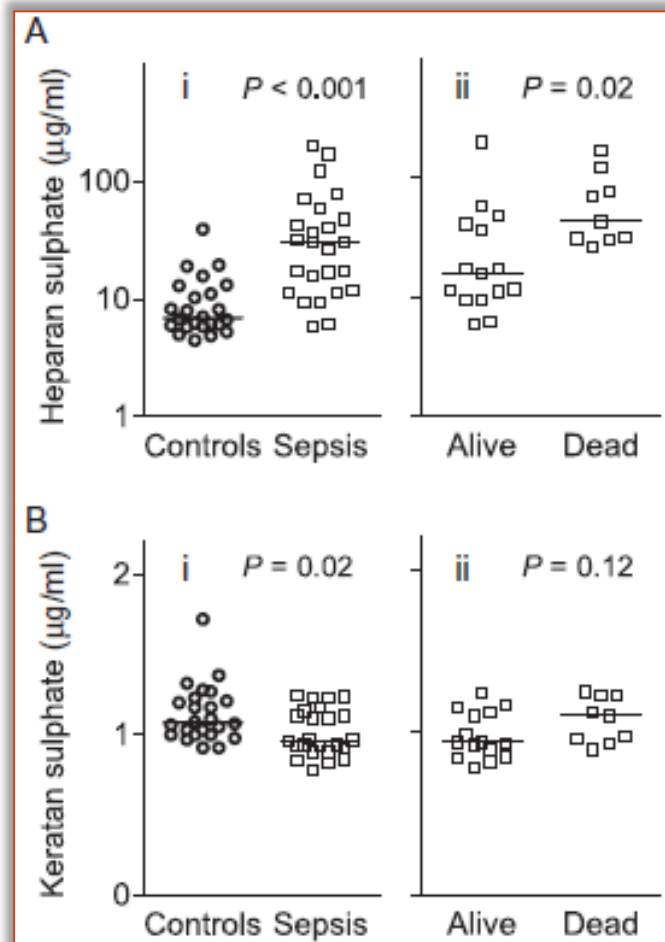
Critical Care 2011, 15(Suppl 3):P22 doi:10.1186/cc10391



Circulating glycosaminoglycan species in septic shock

A. Nelson, I. Berkestedt and M. Bodelsson

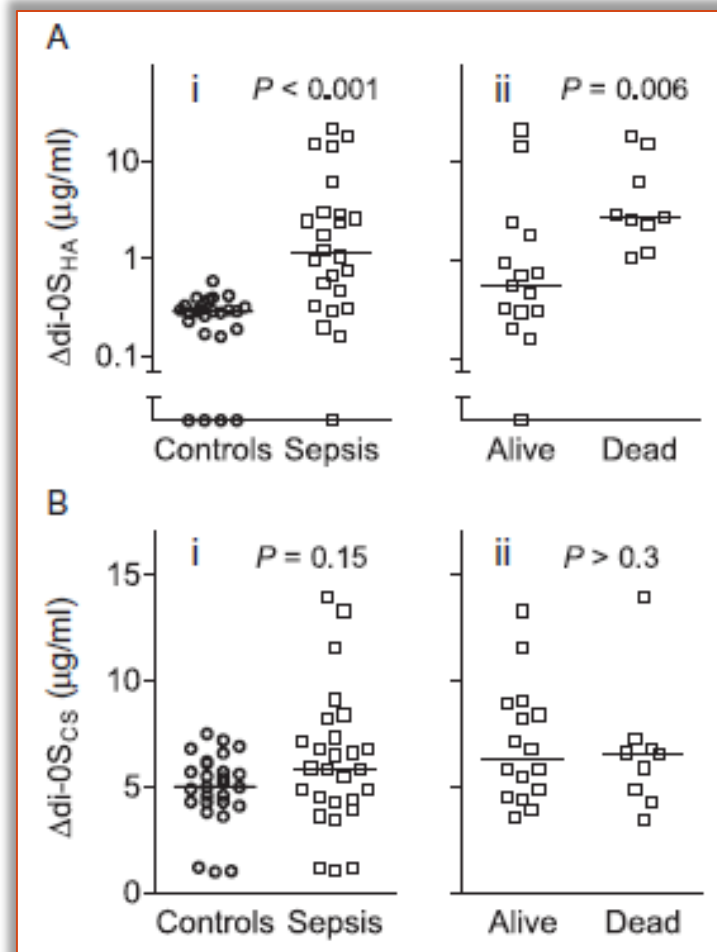
Acta Anaesthesiol Scand 2014; 58: 36–43



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Table 2

Correlations of plasma GAG levels to markers of inflammation.

		IL-6	IL-10	CRP	MPO
HS	<i>r</i>	0.40	0.34	-0.19	0.21
	<i>P</i>	0.06	0.10	> 0.3	> 0.3
Δ di-OS _{HA}	<i>r</i>	0.46	0.47	-0.42	0.26
	<i>P</i>	0.03	0.02	0.05	0.22

CRP, C-reactive protein; GAG, glycosaminoglycan; HS, heparan sulphate; IL-10, interleukin-10; IL-6, interleukin-6; MPO, myeloperoxidase; Δ di-OS_{HA}, 2-acetamido-2-deoxy-3-O-(β -D-glucopyranosyluronic acid)-D-glucose.

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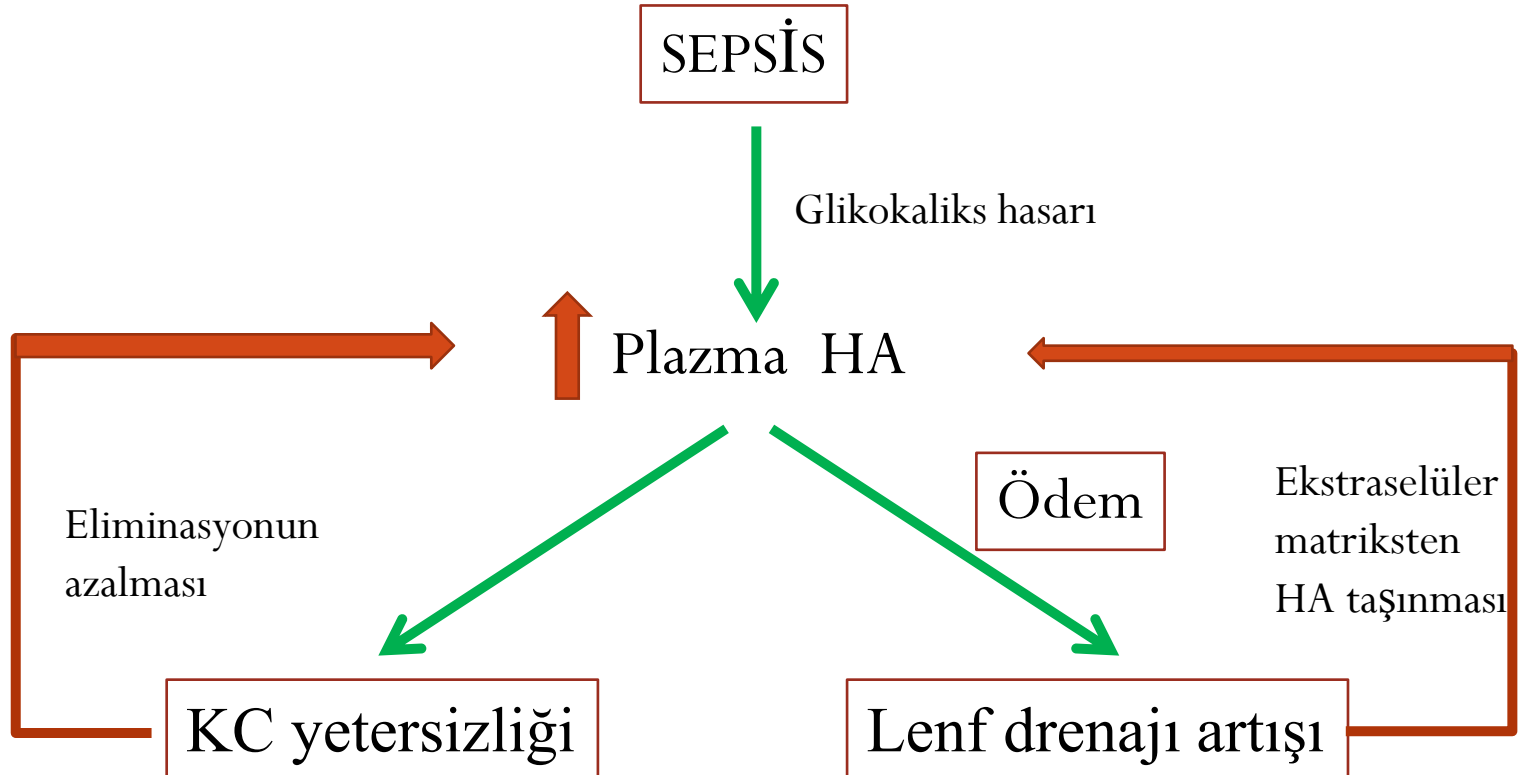
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Glikokaliks Koruması ve Onarımı

- Deneysel hayvan çalışmaları;

Allopurinol, hyaluran

Rubio-Gayosso I. Reactive oxygen species mediate modification of glycocalyx during ischemia-reperfusion injury. *American Journal of Physiology. Heart and Circulatory Physiology* 2006; 290: H2247–56.

Polietilen Glikol

Rosello-Catafau J, Liver graft washout prevents against reperfusion injury: Protective effects on glycocalyx and cytoskeleton. *Transplantation* 2012;

Nitrik oksit

Bruegger D. Exogenous nitric oxide requires an endothelial glycocalyx to prevent postischemic coronary vascular leak in guinea pig hearts. *Critical Care* 2008; 12: R73

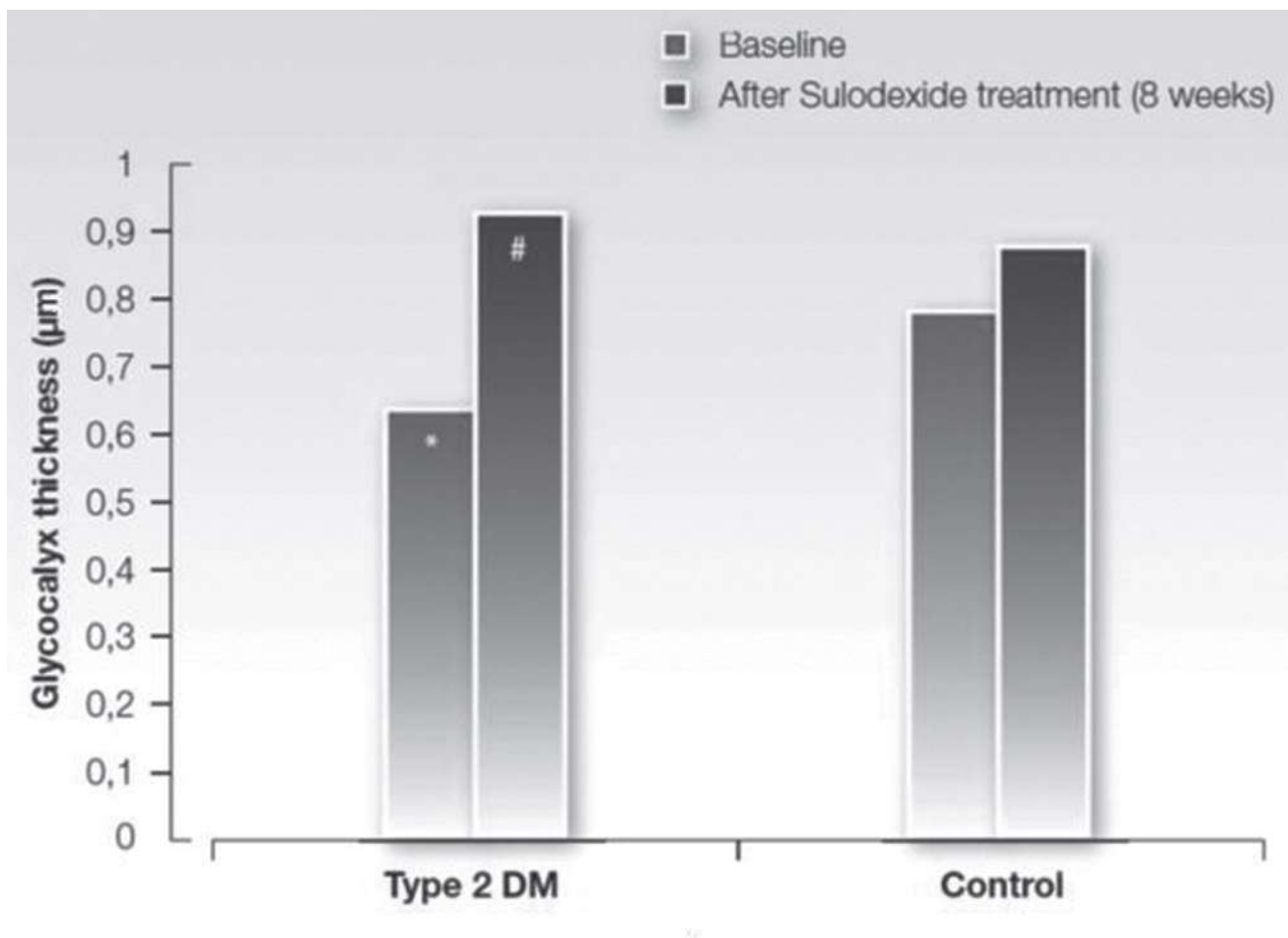
Glycosaminoglycans, proteoglycans and sulodexide and the endothelium: biological roles and pharmacological effects

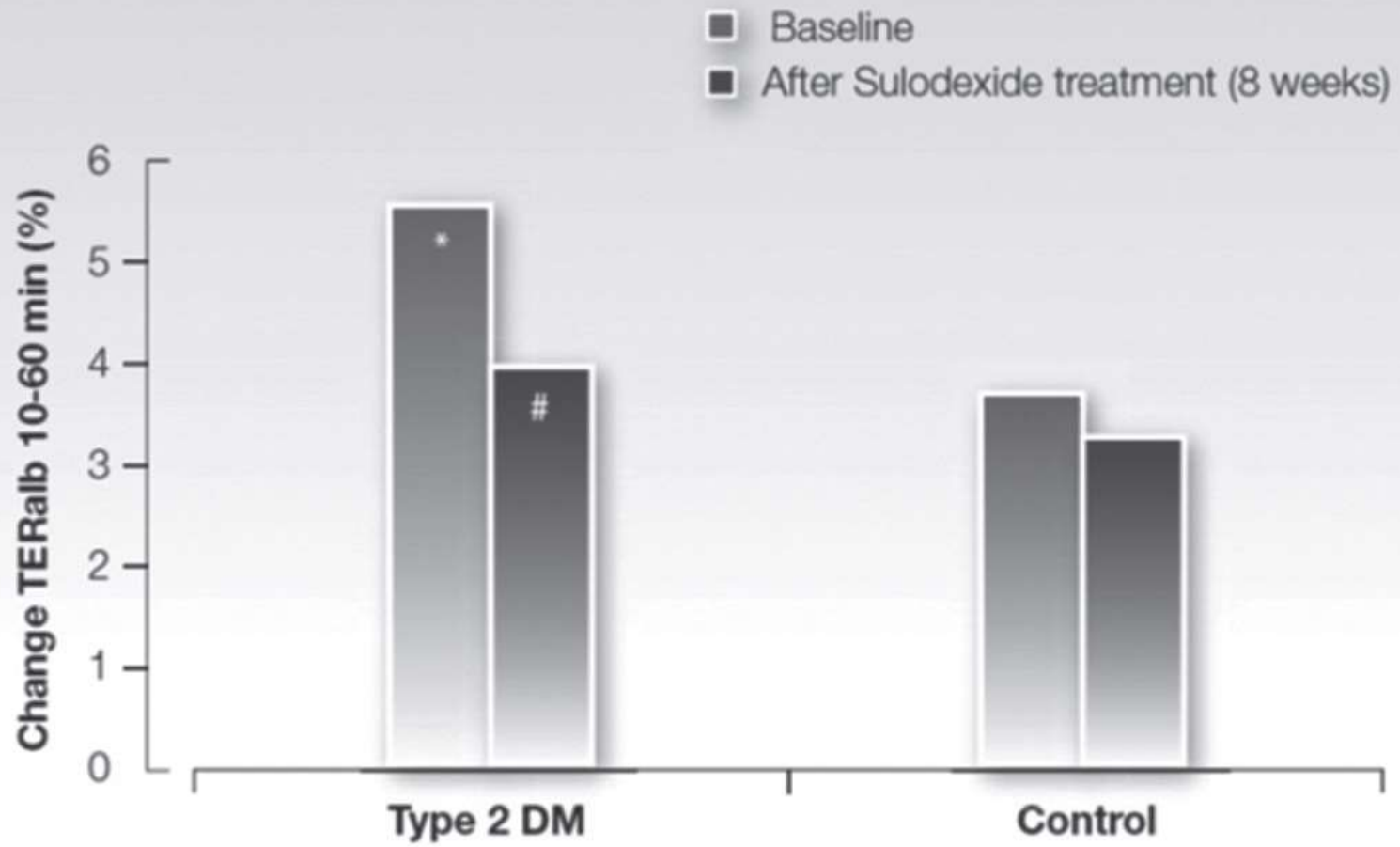
V. MASOLA ^{1, 2}, G. ZAZA ¹, M. ONISTO ², A. LUPO ¹, G. GAMBARO ³

¹Renal Unit, Department of Medicine, University-Hospital of Verona, Verona, Italy; ²Department of Biomedical Sciences, University of Padua, Padua, Italy; ³Division of Nephrology and Dialysis, Columbus-Gemelli Hospital, Catholic University, School of Medicine, Rome, Italy

Int Angiol 2014;33:243-54

- Sulodexide = %80 heparin + %20 dermatan sulfat
- Reatif oksijen ürünü ve IL-6 üretimini azaltır
- Apopitozu engeller
- Heparinaz inhibisyonu
- Glukozun indüklediği glikokaliks hasarını önler



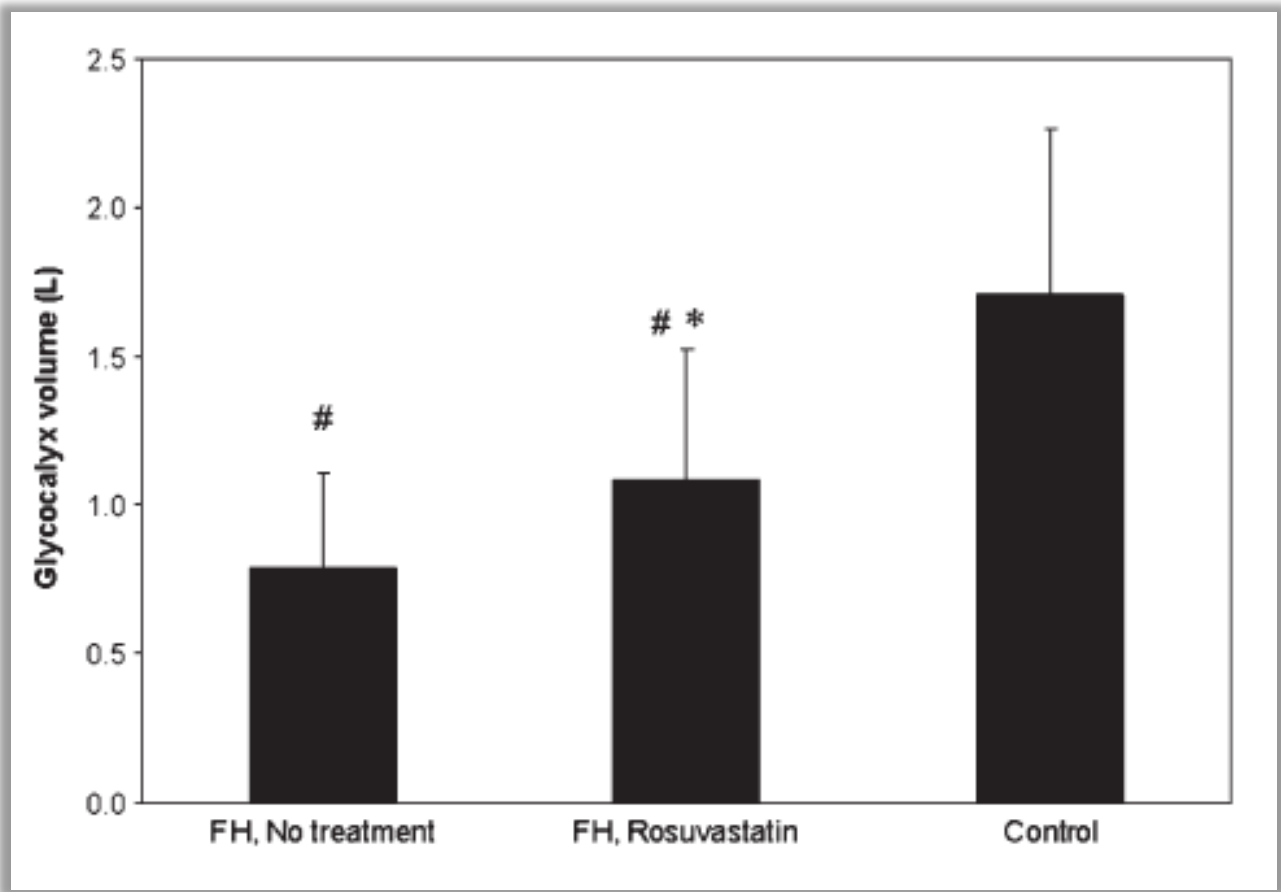


Partial recovery of the endothelial glycocalyx upon rosuvastatin therapy in patients with heterozygous familial hypercholesterolemia

Marijn C. Meuwese,* Hans L. Mooij,* Max Nieuwdorp,* Bart van Lith,* Roos Marck,* Hans Vink,*[†] John J. P. Kastelein,* and Erik S. G. Stroes^{1,*}

J. Lipid Res. 2009. 50: 148–153

- Grup-1:Familiyal hiperkolesterolemi (n:13)
- Grup-2:Normal kolesterol düzeyi (n:13)
- 8 hafta rosuvastatin tedavisi
- Glikokaklis volümü



Bizim alıřmalarımız

- 1-Aık kalp cerrahisinde farklı kardiyopleji tipinin endotelial glikokaliks bütünlüğü üzerine etkisi
- 2- Aık kalp cerrahisinde farklı priming solusyonlarının endotelial glikokaliks bütünlüğü ve mikrosirkülasyon üzerine etkisi
- 3-Böbrek nakli alıcı ve vericilerinde premedikasyonda kullanılan alprozolamın oksidatif stres ve glikokaliks üzerine etkileri

Teşekkürler...