Kalp cerrahisi sonrası yüksek laktat nedenleri

HEPATORENAL SENDROM MU ?

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Ege Üniversitesi Tıp Fakültesi
Anesteziyoloji ve Reanimasyon AD
2013

Konu Akışı

Dekompanse siroz hastasında görülen Hepatorenal Sendrom

Düşük kalp debisine sekonder gelişen Hipoksik Hepatit

The impact of hyperlactatemia on postoperative outcome after adult cardiac surgery

Alexander Kogan · Sergey Preisman · Alex Bar · Leonid Sternik · Jacob Lavee · Ateret Malachy · Dan Spiegelstein · Haim Berkenstadt · Ehud Raanani

Mekanik ventilasyon süresi

YBÜ kalış süresi

Hastanede kalış süresi

Mortalite

d with

Nazan Aksoy, MD,[4]

urgery Forum #2004

Frequency, Risk Factors, and Outcome of Hyperlactatemia After Cardiac Surgery*

Jean-Michel Maillet, MD; Paul Le Besnerais, MD; Manuel Cantoni, MD; Patrick Nataf, MD; Alain Ruffenach, MD; Arrigo Lessana, MD; and Denis Brodaty, MD

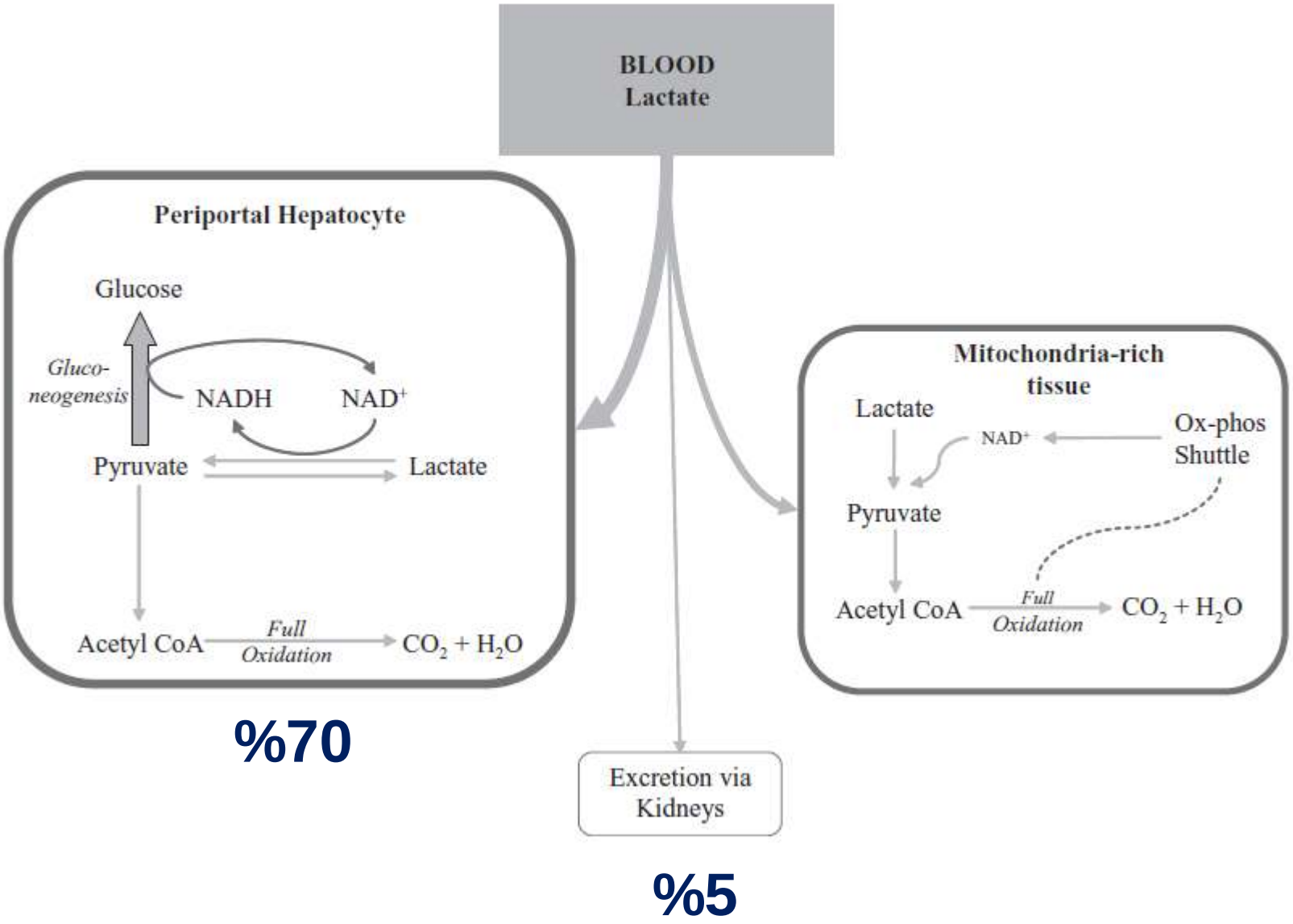
CHEST 2003; 123:1361–1366

Hiperlaktatemi

Artmış üretim

- Hepatik laktat klirensi ↓
- Ekstrahepatik met. ↓
- Renal atılım ↓

Laktat metabolizması



Relationship Between Blood Lactate and Early Hepatic Dysfunction in Acute Circulatory Failure

Bernard De Jonghe, Christine Cheval, Benoit Misset, Jean-François Timsit, Maité Garrouste, Luc Montuclard, and Jean Carlet

Journal of Critical Care, 1999

Akut dolaşım yetm. 92 hasta

29 hasta (%32) → erken hepatik disfonksiyon

(TB>3.5 mg/dl veya SGOT>100 IU/L, ilk 48 saatte)

Table 2. Comparison of Patients With and Without Early Hepatic Dysfunction

Akut dolaşım yetmezliğinde serum laktat yükselmesinde **erken hepatik disfonksiyon** önemli rol oynamaktadır

Blood urea nitrogen (mmol/L)	19 ± 9	15 ± 9	NS
Serum creatinine (μmol/L)	215 ± 127	202 ± 168	NS
Serum lactate (mmol/L)	8.24 ± 6.49	4.29 ± 3.09	$P < .001$
Mortality	79.3%	61.9%	NS

Cardiac Surgery in Patients With End-Stage Liver Disease

Geraldine C. Diaz, DO,* and John F. Renz, MD, PhD†

Child-Turcotte-Pugh sınıflaması

- ✓ Karaciğer fonksiyon bozukluğunun şiddeti ?
- ✓ Postoperatif mortalite ?

	1	2	3
Bilirübin(mg/dL)	< 2	2-3	> 3
Albümin (g/dL)	> 3.5	3-3.5	< 3
PZ uzama (+ sn)	1-4	4-6	> 6
Asit	Yok	Hafif	Belirgin
Ensefalopati	Yok	Gr 1-2	Gr 3-4

Grade	Puan	Cerrahi risk
A	**5-6**	**Düşük**
B	7-9	Orta
C	10-15	Yüksek

Journal of Cardiothoracic and Vascular Anesthesia, 2012

Cardiac Surgery in Patients With End-Stage Liver Disease

Geraldine C. Diaz, DO,* and John F. Renz, MD, PhD†

Table 2. Cardiac Surgical Morbidity and Mortality Correlate With Severity of Liver Disease by Child-Pugh Class

Study	Year	n	A (%)	B (%)	C (%)
Morbidity					
Klemperer et al[18]	1998	13	25	100	—
Bizouarn et al[11]	1999	12	50	100	—
Hayashida et al[19]	2004	18	60	100	100
Suman et al[24]	2004	44	10	66	100
Lin et al[20]	2005	18	39	80	80
An et al[21]	2007	24	53	100	100
Filsoufi et al[25]	2007	27	22	56	100
Mortality					
Klemperer et al[18]	1998	13	0	80	—
Bizouarn et al[11]	1999	12	20	50	—
Hayashida et al[19]	2004	18	0	50	100
Suman et al[24]	2004	44	3	42	100
Lin et al[20]	2005	18	0	0	
An et al[21]	2007	24	6	67	100
Filsoufi et al[25]	2007	27	11	18	67
Vanhuyse et al[31]	2012	34	18	40	100

Child A

Morbidite %10 - 60

Mortalite %0 - 20

Journal of Cardiothoracic and Vascular Anesthesia, 2012

Hepatorenal Sendrom (HRS)

Sıklıkla dekompanse sirozlu ve daha seyrek olarak akut karaciğer yetersizliği olan hastalarda görülen, ciddi renal vazokonstriksiyonla karakterize akut renal yetersizlik

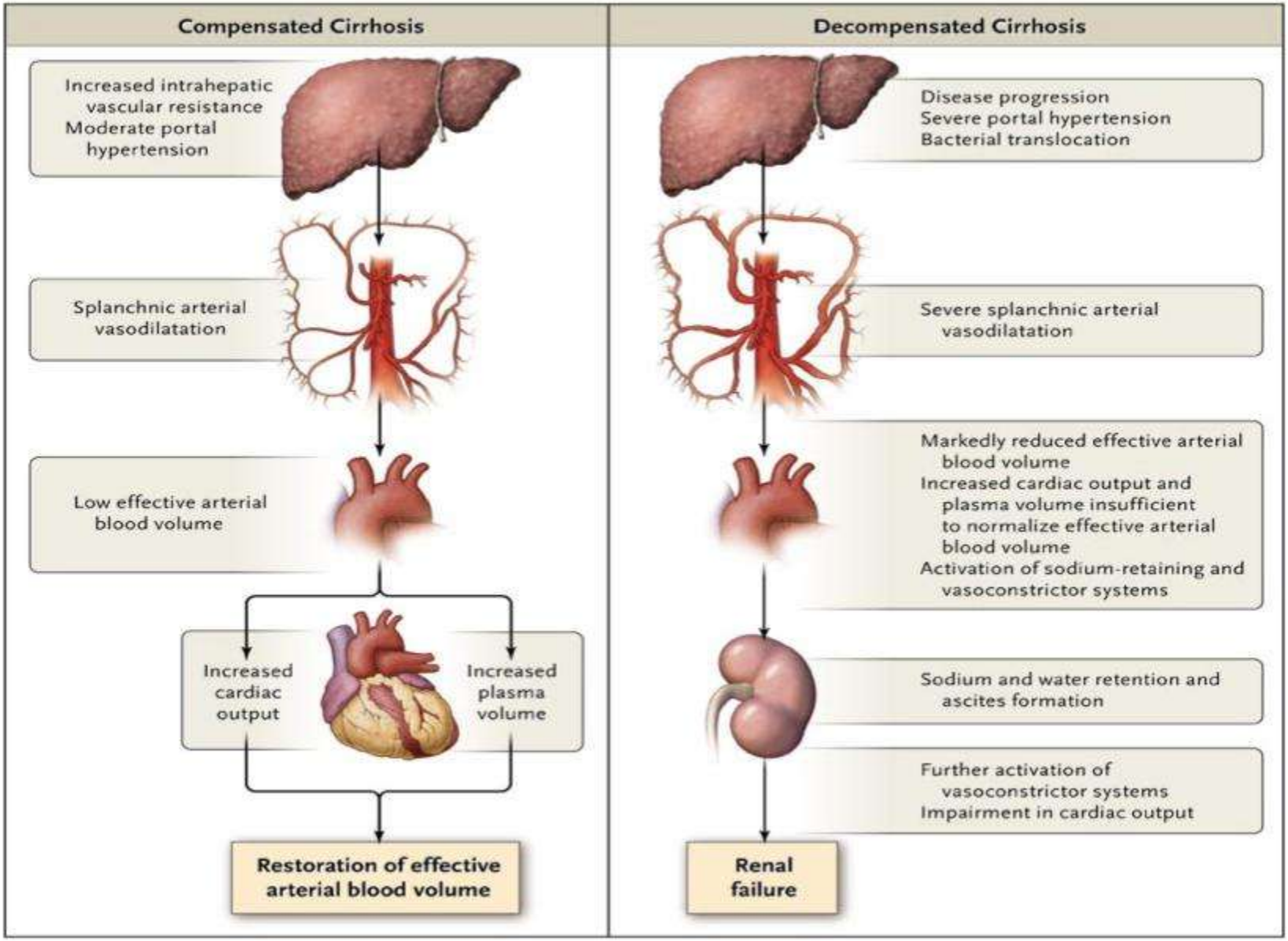
HRS → fonksiyonel bir bozukluk

Dekompanse siroz hastalarında HRS gelişme sıklığı:

1 yıl / %18

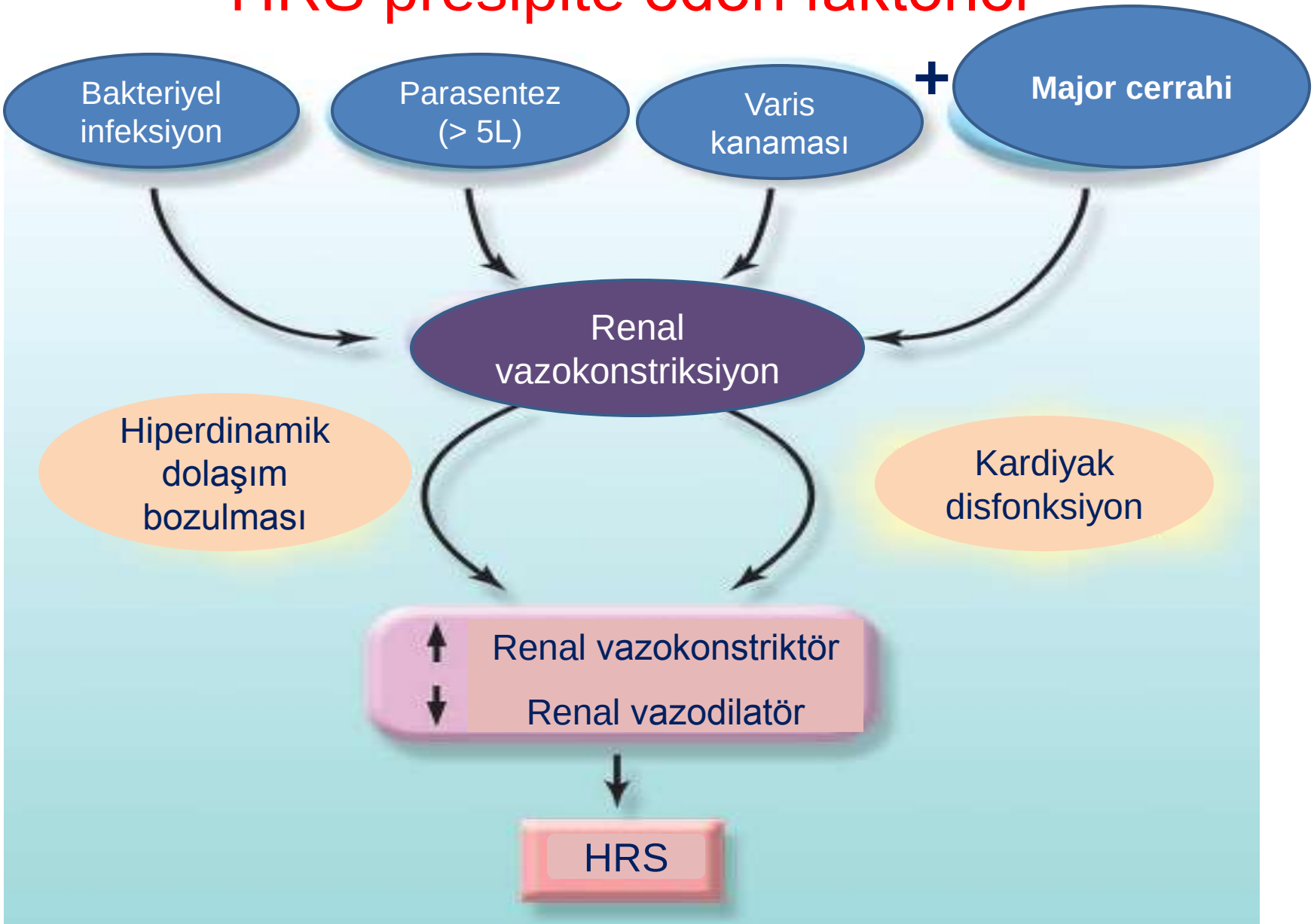
5 yıl / %40

HRS Patofizyolojisi



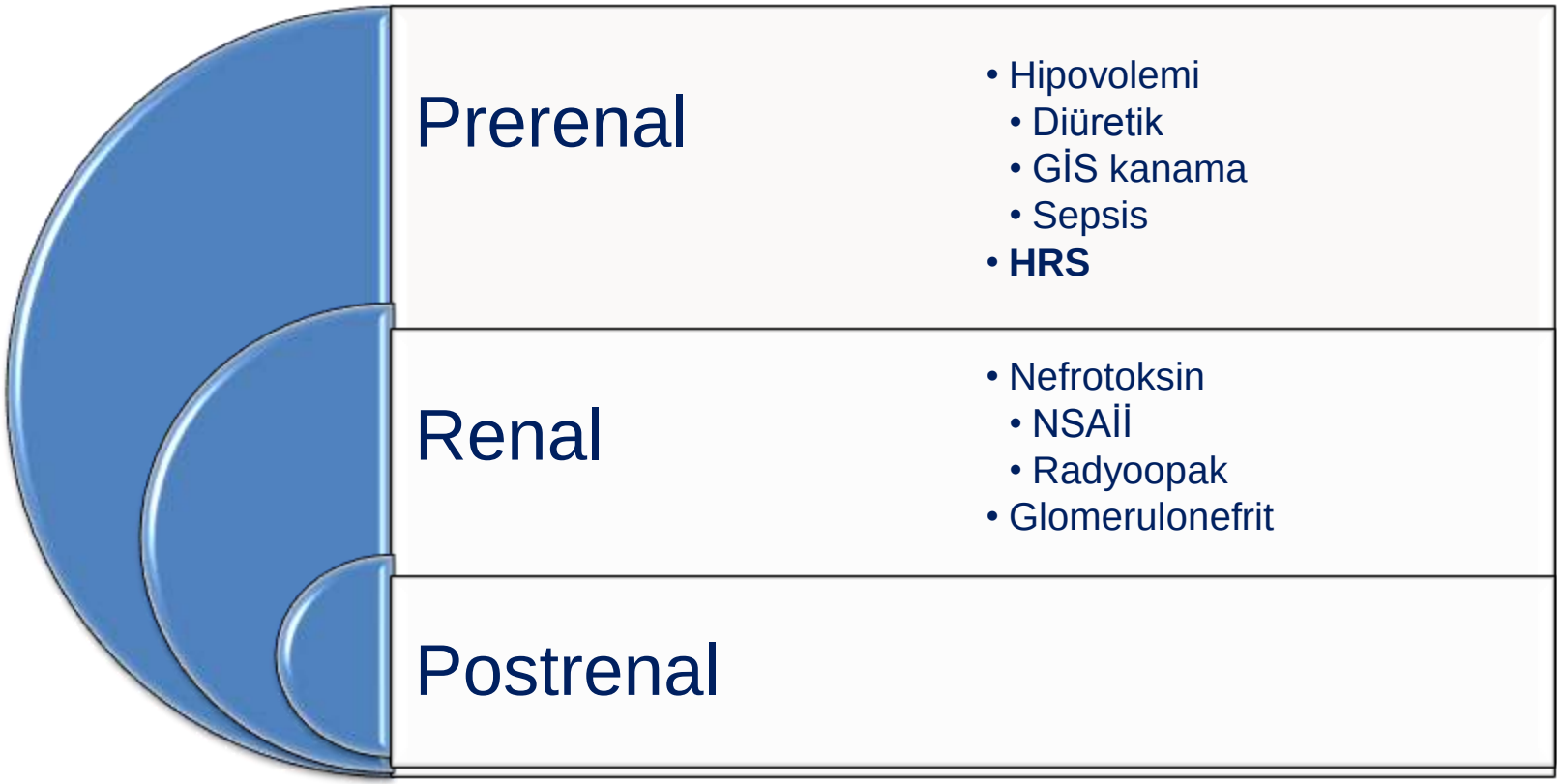
Am J Kidney Dis, 2012

HRS presipite eden faktörler



HRS tanısı,

spesifik bir test bulunmadığı için sirozda akut böbrek hasarına neden olan diğer hastalıkların dışlanmasına dayanmaktadır



HRS tanı kriterleri (2007)

- ✓ Dekompanse siroz (asiti olan hasta)
- ✓ Serum kreatinin düzeyi > 1.5 mg/dL (133 µmol/L)
- ✓ DÜ kesilmesi ve yeterli volüm replasmanına rağmen serum kreatinin düzeyinde azalma olmaması
- ✓ Hastanın şokta olmaması
- ✓ Nefrotoksik ilaç kullanımı olmaması
- ✓ Parankimal böbrek hastalığının olmaması

Salerno F. Gut, 2007

HRS tipleri

Tip 1 HRS

- Böbrek fonksiyonlarında akut, progresif azalma

  (2 haftadan daha kısa süre icinde kreatinin > 2.5 mg/dL)
- Presipite edici faktör sıklıkla (+)
- Tedavisiz sağkalım oranı <2 hafta

Tip 2 HRS

- Daha ılımlı (kreatinin 1.5 – 2.5 mg/dL)
- DÜ direncli asit (+)
- Sağkalım ~6 ay

HRS tedavisi

Vazokonstriktörler

- ✓ Terlipresin
- ✓ Midodrine
- ✓ Norepinefrin

\+ Albumin

KC Transplantasyonu

Cerrahi tekniklerdeki ve miyokardiyal koruma yöntemlerindeki gelişmelere rağmen KPB sonrası gelişen **Düşük Kalp Debisi Sendromu** önemli bir sorundur

- Kros klemp sırasında oluşan miyokard iskemisi
- Reperfüzyon hasarı
- İnflamatuvar reaksiyon
- Pıhtılaşma sistem aktivasyonu sonucu gelişir

When the Heart Kills the Liver: Acute Liver Failure in Congestive Heart Failure

F. H. Saner[1], M. Heuer[1], M. Meyer[1], A. Canbay[2], G. C. Sotiropoulos[1], A. Radtke[1], J. Treckmann[1], S. Beckebaum[1], C. Dohna-Schwake[2], S. W. Oldedamink[3,4], A. Paul[1]

Eur J Med Res (2009) 14: 541-546

202 Akut kc yetm /5 yıl
13 hasta KKY'ne bağlı akut kc yetm

Mortalite %54 /ilk 4 günde

Value	Admission	Day 7
AST (U/L)	4029 ± 3514	1043 ± 1013*
ALT (U/L)	2685 ± 2088	1193 ± 1068
Bilirubin (U/L)	4.3 ± 3.1	2.2 ± 1.3
INR	2.4 ± 1.3	1.7 ± 0.5
HR (1/min)	105 ± 26	115 ± 28
MAP (mmHg)	71 ± 15	73 ± 9
CVP (mmHg)	16 ± 5	11 ± 2 *
CI (L*min-1*m^2)	1.9 ± 0.9	3 ± 1*
MPAP (mmHg)	40 ± 19	27 ± 7
PCWP (mmHg)	20 ± 10	15 ± 5
SVR (dyn*sec*cm-5)	1713 ± 525	922 ± 236
PVR (dyn*sec*cm-5)	327 ± 146	202 ± 49
Noradrenaline (µg/kg/min)	0.9 ± 0.6	0.2 ± 0.1*

*$P < 0.05$

Hipoksik Hepatit

1901 (Mallory) 1190 otopsi → 95 vakada

santral ven etrafında hepatik nekroz (santral nekroz)

Sentrilobüler kc hücre nekrozu

↓

Hipoksik Hepatit

Henrion J. Liver International 2012

Hipoksik Hepatit

Altta yatan akut kardiyak, dolaşımsal veya solunumsal yetmezlik duruma sekonder **serum transaminazlarında ani, masif ve geçici artış**la karakterize akut kc hasarı

Henrion J. Liver International 2012

YBÜ %1 - 12

Kalp cerrahisi sonrası %1

Table 2. Prevalence of hypoxic hepatitis in intensive care units

Author, date (ref.)	Fuchs 1998 (25)	Henrion 2003 (2)	Birrer 2007 (3)	Fuhrmann 2009 (5)	Raurich 2010 (7)
Setting	Tertiary centre	General hospital	1 Tertiary centre 1 General hospital	3 Tertiary centres	1 Tertiary centre
Study schedule	Retrospective	Prospective	Retrospective	Prospective	Retrospective
Inclusion period	39 months 1993–1996	10 years 1983–1992	13 years 1990–2002	22 months 2005–2006	8 years 2001–2008
S-AT x ULN*	8	20	10	20	20
No. of admissions	2155	15 619	32 209	984	7674
No. of HH†	33	142	322	118	182
Prevalence (%)	1.5	0.9	1	11.9	2.4

Henrion J. Medicine, 2003
Birrer R. Intern Med, 2007
Fuhrmann V. Intensive Care Med, 2009
Raurich JM. J Anesth 2011

KC hipoksik strese karşı iyi korunmuştur

- ✓ Dual kan akımı (portal ven - hepatik arter)
- ✓ Kc sinüzoidlerinin özel yapısı
- ✓ Hepatik arter tampon yanıtı

Hepatik kan akımı

hCO = %25

hDO2 = %50

hCO = %75

hDO2 = %50

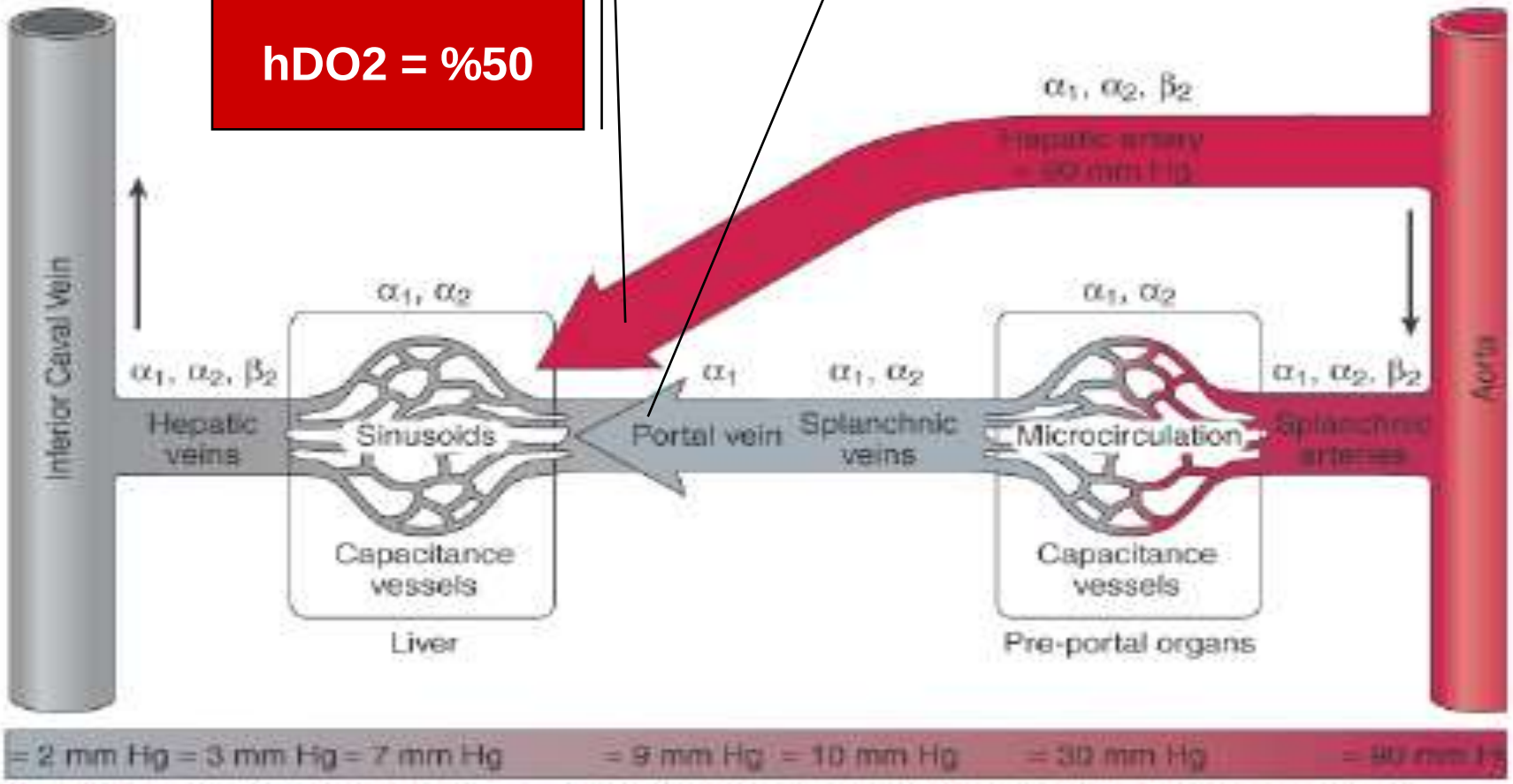


Figure 19-5 Adrenoceptor subtypes (α_1, α_2, β_2) and intravascular pressures throughout the splanchnic circulation. *Splanchnic arteries* represent all arterial vessels of the pre-portal organs; *splanchnic veins* represent the pooled venous

Hipoksik Hepatit - Patofizyoloji


KPB hemodinamik etkileri
Nonpulsatil akım
Düşük KD
Hipotansiyon
Hipoperfüzyon
KC HASARI ?
Hipotermi
Kanama - hipovolemi
İskemi-reperfüzyon
Artmış sempatik aktivite

Hipoksik Hepatit - Patofizyoloji

Düşük kalp debisi ve DO_2 azalması

Sağ kalp yetm. bağlı kc pasif konjesyonu

İskemi - reperfüzyon hasarı

REVIEW ARTICLE

Hypoxic hepatitis

Jean Henrion

CVP ↑

CI, DO2, HKA ↓

Table 4. Hemodynamic assessment in hypoxic hepatitis caused by cardiac failure (results expressed as medians)

Author (ref.)	J. Henrion (2)	B. Birrer (3)	Normal values (36)
No. of cases	73	198	–
CVP (cm H_2O)	21	20	1–9
CI (L/min.m^2)	1.97 (n = 34)	1.91	2.8–3.6
DO_2 (ml/min.m^2)	350 (n = 34)	325	520–720
PaO_2 (mmHg)	64	84	80–98
HBF (ml/min.m^2)	795 (n = 18)	778	2100*

Henrion J. Medicine 2003
Birrer R. Intern Med 2007

Hipoksik Hepatit - tanı kriterleri

- ✓ Altta yatan akut kardiyak, dolaşımsal veya solunumsal yetmezlik
- ✓ Aminotransferazlarda ani ve geçici olarak bazal değerin 20 katından fazla artış olması
- ✓ Karaciğer hasarına neden olabilecek başka bir neden olmaması (viral ya da toksik hepatit gibi)

KC biyopsisi ➡ **sentrilobüler nekroz**

US ➡ dilate kc venleri

HH sırasında transaminazlar - PA

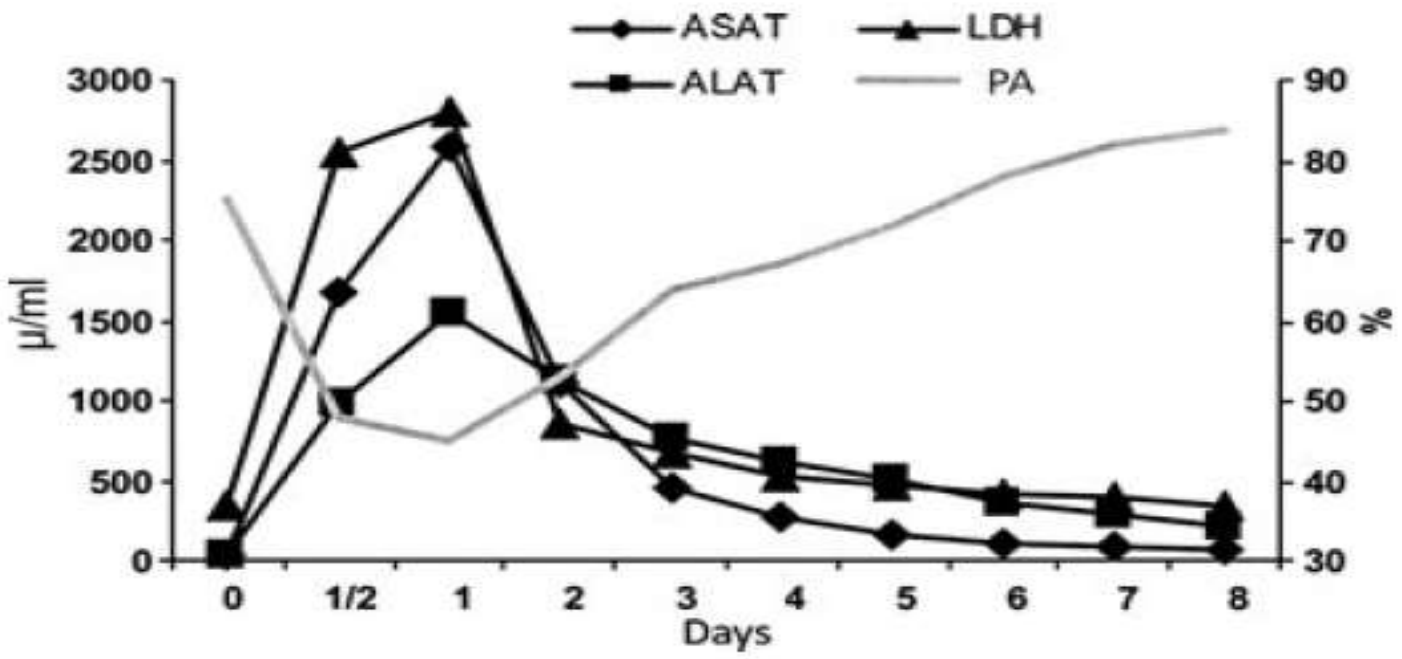


Fig. 2. Pattern of enzyme and prothrombin activities in 25 cases of hypoxic hepatitis with initial enzyme activities less than 2× upper limit of normal, survival of at least 8 days and complete set of data (values are reported in means). ALAT, alanine aminotransferase; ASAT, aspartate aminotransferase; LDH, lacticodehydrogenase; PA, prothrombin activity.

Henrion J. Liver International 2012

Hypoxic hepatitis – epidemiology, pathophysiology and clinical management

Valentin Fuhrmann[1], Bernhard Jäger[1], Anna Zubkova[2], Andreas Drolz[1]

Table 2. Laboratory characteristics* in patients with hypoxic hepatitis

Variable	Henrion et al. [6]	Birrer et al. [7]	Fuhrmann et al. [8]
Number of patients	138	293	117
AST (U/l)	2155 (455–15400)	2288 (1768–2715)	2507 (701–27560)
ALT (U/l)	1645 (237–8590)	1803 (1493–2084)	1348 (135–12452)
LDH (U/l)	2750 (105–9040)	3545 (3224–3787)	2826 (324–27220)
Bilirubin (mg/dl)	2.1 (0.4–22.5)	2.2 (1.8–2.5)	2.6 (0.4–49.5)
PTT (%)	36 (6–89)	n.a.	31 (5–87)
Lactate (mmol/l)	5.6 (0.8–32)	5.5 (4.6–9.5)	9.5 (1.1–26)

ansaminases; *LDH* lactate dehydrogenase; *PTT* prothrombin time.

AST, ALT

LDH

Bilirübin

Laktat

Henrion J. Medicine, 2003
Birrer R. Intern Med, 2007
Fuhrmann V. Intensive Care Med, 2009

REVIEW ARTICLE

Hypoxic hepatitis

Jean Henrion

Author date (ref.)	Henrion 2003 (2)	Birrer 2007 (3)
No. of cases	142	322
Inclusion period	1983–1992	1990–2002
M/F	2	2.4
Age	68.5	70.3
Shock (% cases)	55	51
Pe Peak ASAT (x ULN)*	79.6†	44.2
Peak ALAT (x ULN)*	50.6†	28.6
Peak LDH (x ULN)*	21.9†	15.2
Prothrombin activity	37.5%†	22 sec
Peak creatinine (mg/dl)	3.1†	3
Peak bilirubin (mg/dl)	3.1†	2.2
Hypoglycaemia	<70 mg/dl 2.8%	<60 mg/dl 2.8%
In-hospital mortality (%)	52.8	45
1-year survival (%)	28.3	23.5

Kreatinin

>2 mg/dL %65

>5 mg/dL %15

Henrion J. Medicine 2003
Birrer R. Intern Med 2007

Prognoz

- ✓ KC hasarı şiddeti ve süresi
  - INR>2
  - Yüksek AST >24 saat
- ✓ Vazopressör tedavi
- ✓ Şok (+)

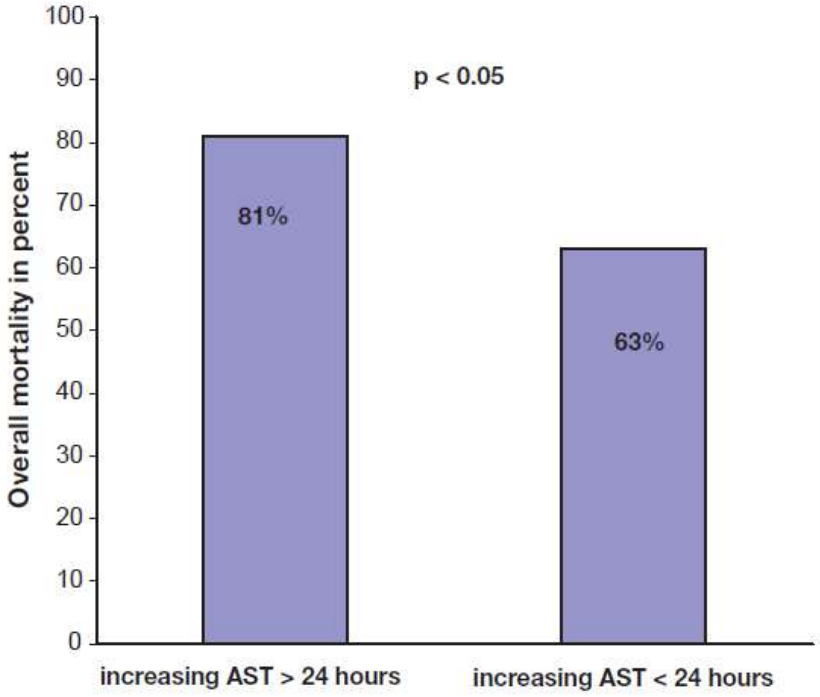


Fig. 3. Overall mortality in patients with hypoxic hepatitis ($n = 117$) depending on the duration of liver injury [8]. AST > 24 hours increasing serum aspartate transaminases levels for more than 24 hours as indicator of prolonged onset of hypoxic hepatitis in contrast to AST < 24 hours

HH tedavisi = Altta yatan hastalık tedavisi

Yeterli perfüzyon ve kalp debisinin sağlanması

İnotropik ilaçlar, vazopressör destek, IABP, ECLS

KC destek ted ?

Severe Ischemic Early Liver Injury After Cardiac Surgery

Jai S. Raman, FRACS, Kazuhiro Kochi, MD, Hiroshi Morimatsu, MD,
Brian Buxton, FRACS, and Rinaldo Bellomo, MD

Ann Thorac Surg 2002;74:1601–6

Üç yılda kalp cerrahisi geçiren 1800 hasta

Ciddi iskemik erken kc hasarı: Postop. 48 saat içinde serum ALT > 500 IU/L

20 hasta	→	RF
13 KABG		insidans
3 kapak + KABG		hemodinamik özellikleri
4 kapak		mortalite

Severe Ischemic Early Liver Injury After Cardiac Surgery

Jai S. Raman, FRACS, Kazuhiro Kochi, MD, Hiroshi Morimatsu, MD, Brian Buxton, FRACS, and Rinaldo Bellomo, MD

Table 1. Comparison Between the Patients With Severe Ischemic Early Liver Injury and Controls

	SIELI (Group I)	Controls (Group II)	ARF/Shock (Group III)
Age	65.7 ± 10.7	68.5 ± 12.1	70.1 ± 12.5
Male/Female	8/12	13/7	15/5
Parsonnet scores	12.5 ± 6.1*	14.3 ± 6.6	16.9 ± 6.43*
NYHA classification	3.4 ± 0.7*	3.2 ± 1.2	2.3 ± 0.81*
Diabetes mellitus	13*,†	6†	4*
Hypertension	16*,†	10†	8*
Cardiopulmonary bypass period (min)	146.6 ± 52.8*,†	110.7 ± 38.2†,‡	230.4 ± 105.0*,‡
Aortic cross-clamp period (min)	95.9 ± 37.6*	80.5 ± 28.8‡	142.1 ± 69.7*,‡
Postoperative low output status[a]	13†	4†	13‡
Extracorporeal life support/intraaortic balloon pumping	4/4	1/0	3/7
Preoperative ALT (alanine amino transferase) (IU/L)	34.1 ± 21.4	36.0 ± 30.4	49.6 ± 75.0
Postoperative maximum ALT (IU/L)	2523 ± 1843*,†	44.0 ± 2.31†	138 ± 135*
Preoperative creatinine (μmol/l)	137 ± 47†	83 ± 40†,‡	157 ± 127‡
Postoperative creatinine (μmol/l)	227 ± 104†	122 ± 42†,‡	235 ± 125‡
Postoperative creatine phosphokinase (IU/L)	3640 ± 3956†	1363 ± 1341†	2298 ± 2010
Mechanical ventilation for > 48 hours	15†	3†	12‡
Death	13†	1†,‡	9‡

Ann Thorac Surg 2002;74:1601–6

Severe Ischemic Early Liver Injury After Cardiac Surgery

Jai S. Raman, FRACS, Kazuhiro Kochi, MD, Hiroshi Morimatsu, MD, Brian Buxton, FRACS, and Rinaldo Bellomo, MD

Table 2. Hemodynamic Features of Affected Subjects and Controls[a]

	SIELI (I)	Controls (II)	ARF/Shock (III)	*p* Value
Lowest cardiac index (L/min/m^2)	1.86 ± 0.28	2.35 ± 0.46	2.20 ± 0.62	*0.0035; †NS ‡NS
Highest PAOP (mm Hg)	19.1 ± 3.8	15.1 ± 4.7	22.5 ± 5.87	*0.019 †NS ‡0.01
Highest RAP (mm Hg)	16.6 ± 5.7	12.8 ± 0.3	17.1 ± 3.9	*0.009 †NS ‡0.007
Mean radial arterial pressure (mm Hg)	80.1 ± 15.7	80.2 ± 13.4	72.8 ± 9.3	*NS †NS ‡NS
Peak norepinephrine dose (μg/min)	25.4 ± 22.4	4.95 ± 10.2	34.8 ± 36.4	*0.0004 †NS ‡0.0003
Peak milrinone (μg/kg/min)	0.356 ± 0.290	0.163 ± 0.294	0.352 ± 0.156	*0.005 †NS ‡0.005

Kİ ⇩

PCWP – CVP ⇧

Vazopressör ve inotrop gereksinimi ⇧

Severe Ischemic Early Liver Injury After Cardiac Surgery

Jai S. Raman, FRACS, Kazuhiro Kochi, MD, Hiroshi Morimatsu, MD, Brian Buxton, FRACS, and Rinaldo Bellomo, MD

ALT

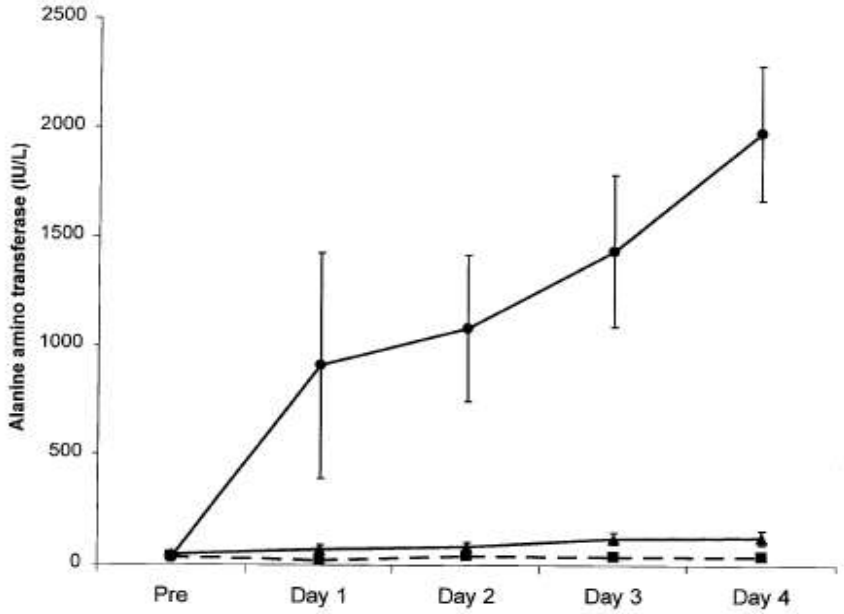


Fig 1. Changes in alanine amino transferase levels in the immediate postoperative period. No significant changes occurred in preoperative controls (square) *and acute renal failure/shock patients* (triangle)*, but there was a marked and rapid rise in affected patients* (circle) *to a mean level more than 3000 IU/L that peaked at day 3 and then returned to baseline over several days.* (Pre = *preoperative.*)

KREATİNİN

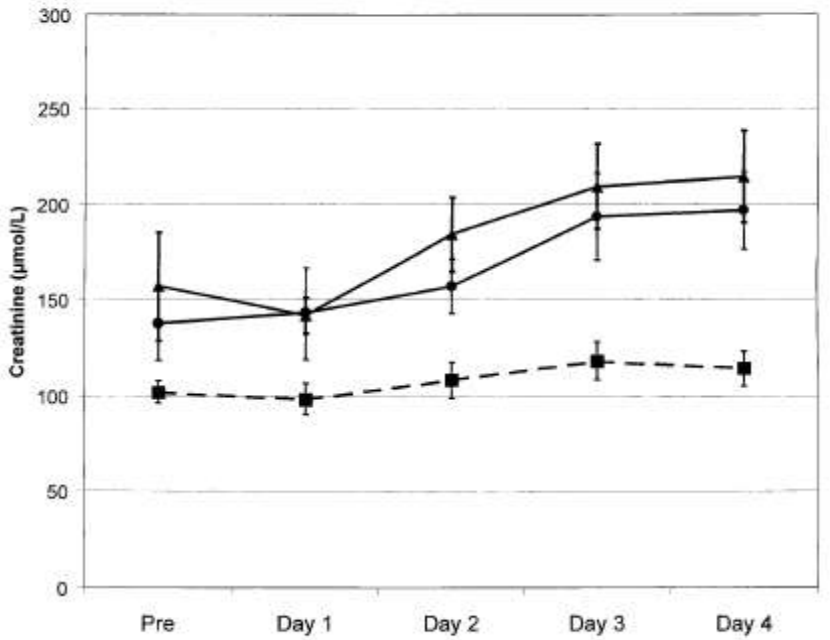


Fig 3. Serum creatinine concentration in patients with severe ischemic early liver injury after cardiac surgery (circle) *and acute renal failure/shock* (triangle) *was significantly greater than in preoperative controls* (square) *in the immediate postoperative period.* (Pre = *preoperative.*)

Severe Ischemic Early Liver Injury After Cardiac Surgery

Jai S. Raman, FRACS, Kazuhiro Kochi, MD, Hiroshi Morimatsu, MD, Brian Buxton, FRACS, and Rinaldo Bellomo, MD

- ✓ Ciddi iskemik karaciğer hasarı insidansı %1.1
- ✓ Düşük KD ve yüksek dolum basınçları, KC hasarı patogenezinde **azalmış perfüzyon ve konjesyon**un etkili olduğunu göstermekte
- ✓ RF: Preop. kalp yetm, DM, HT öyküsü ve postoperatif düşük KD
- ✓ Mortalite %65

SONUÇ

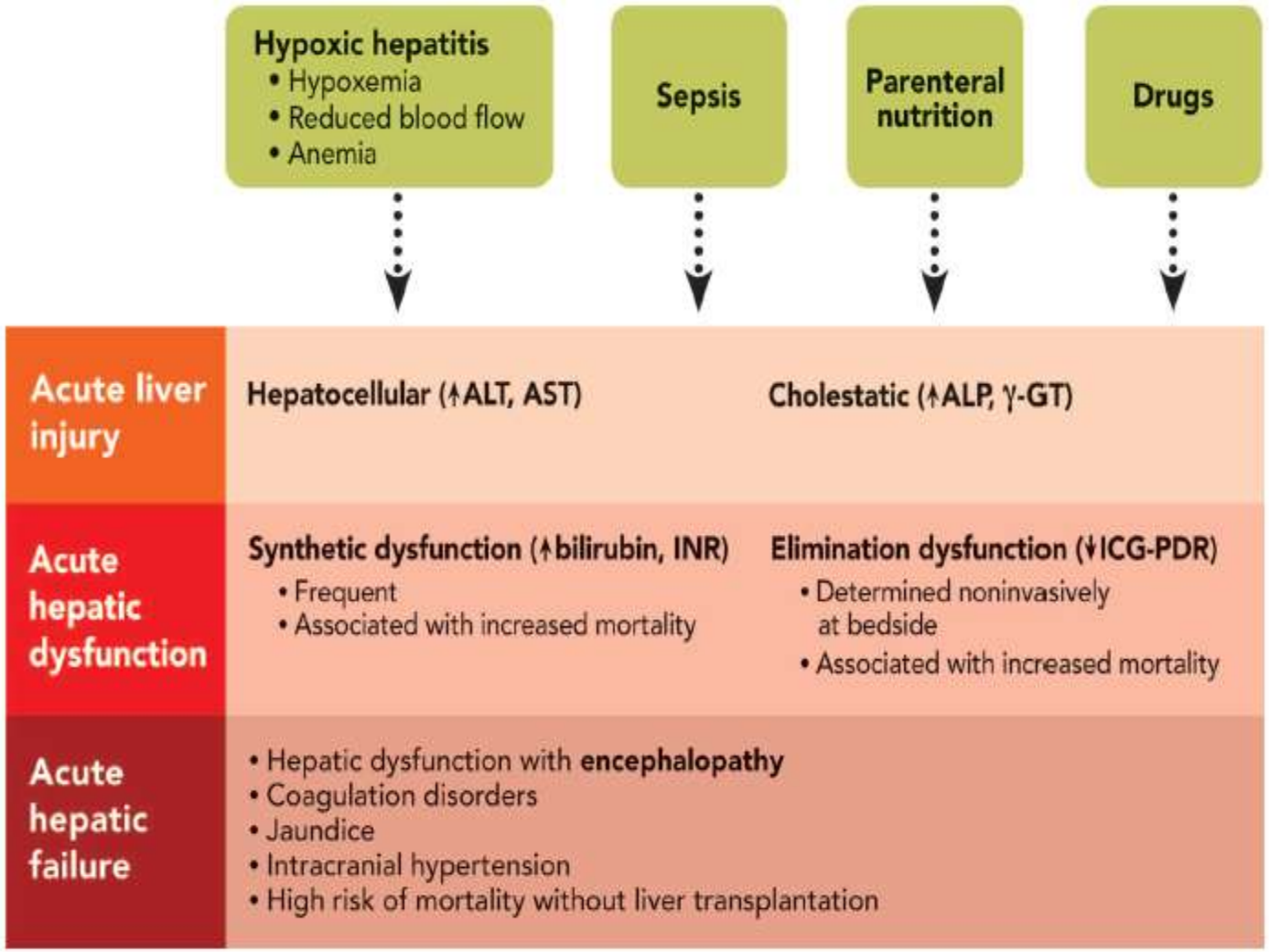
- ✓ Kalp cerrahisi sonrası laktat yüksekliği morbidite ve mortaliteyi artırmaktadır
- ✓ Postoperatif kan laktat düzeyi monitörizasyonu durumu kötüye giden hastayı göstermesi ve erken önlem alınması açısından önemlidir
- ✓ HRS, sıklıkla dekompanse sirozlu hastalarda görülen, ciddi renal vazokonstriksiyonla karakterize akut renal yetersizliktir

SONUÇ

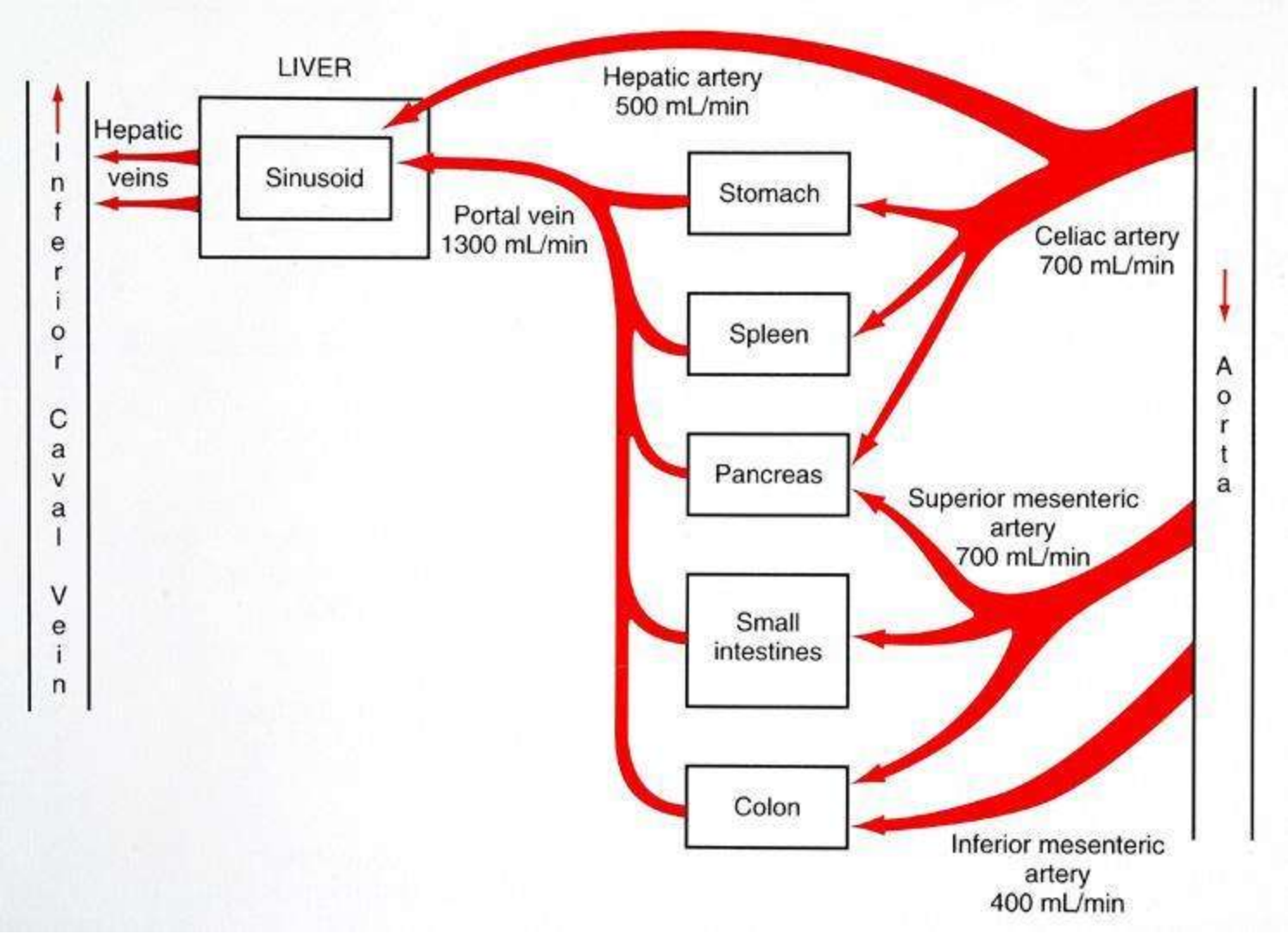
- ✓ Hipoksik hepatit, atta yatan akut kardiyak, dolaşımsal veya solunumsal yetmezlik duruma sekonder serum transaminazlarında ani, masif ve geçici artışla karakterize akut kc hasarıdır

- ✓ Kalp cerrahisi sonrası düşük kalp debisine bağlı hipoksik hepatit yüksek mortalite riski taşımaktadır. Erken tanı ve altta yatan nedene yönelik tedavinin hızla başlanması iyi prognoz açısından önemlidir

İLGİNİZ İÇİN TEŞEKKÜRLER


Hypoxic hepatitis
• Hypoxemia
• Reduced blood flow
• Anemia
Sepsis
Parenteral nutrition
Drugs
Acute liver injury
Hepatocellular (↑ALT, AST)
Cholestatic (↑ALP, γ-GT)
Acute hepatic dysfunction
Synthetic dysfunction (↑bilirubin, INR)
• Frequent
• Associated with increased mortality
Elimination dysfunction (↓ICG-PDR)
• Determined noninvasively at bedside
• Associated with increased mortality
Acute hepatic failure
• Hepatic dysfunction with encephalopathy
• Coagulation disorders
• Jaundice
• Intracranial hypertension
• High risk of mortality without liver transplantation

Splanchnic Circulation



Diagnostic Criteria

- Minor : (not necessary for diagnosis)

- İdrar < 500 ml/gün
- İdrar Na < 10 mmol/gün
- İdrar osmolaritesi > plazma osmolaritesi
- Urine red cells < 50/ hpf
- Serum sodium < 130 mmol/L

Box 3. Pharmacologic Treatment of HRS

Vasoconstrictors

- Terlipressin: 1 mg/4-6 h intravenously; the dose is increased up to a maximum of 2 mg/4-6 h after 3 days if there is no response to therapy, defined by a decrease in serum creatinine >25% of pretreatment values. Response to therapy is indicated by a marked decrease in the high serum creatinine levels, at least <1.5 mg/dL (<133 μmol/L). Treatment is usually given from 5-15 days
- Midodrine: 7.5 mg orally 3×/d, increased to 12.5 mg 3×/d if needed
- Octreotide: 100 μg subcutaneously 3×/d, increased to 200 μg 3×/d if needed
- Norepinephrine: 0.5-3 mg/h as continuous intravenous infusion aimed at increasing mean arterial pressure by 10 mm Hg. Treatment is maintained until serum creatinine decreases <1.5 mg/dL (<133 μmol/L)

Albumin administration

Concomitant administration of albumin together with vasoconstrictor drugs (1 g/kg body weight at day 1 followed by 20-40 g/d)