

Journal of Clinical and Basic Cardiology

An Independent International Scientific Journal



Journal of Clinical and Basic Cardiology 2000; 3 (1), 35-38

Cardiogenic hepatic injury-renal impairment

Naschitz JE, Abinader EG, Elias N, Sabo E, Yeshurun D
Zuckerman E

Homepage:

www.kup.at/jcbc

**Online Data Base Search
for Authors and Keywords**

Cardiogenic Hepatic Injury-Renal Impairment

J. E. Naschitz¹, N. Elias¹, E. Zuckerman¹, E. Sabo², E. G. Abinader³, D. Yeshurun¹

Cardiogenic hepatic injury-renal impairment (CAHIRI) was defined by us as an acute complication, manifesting within 48 hours after an episode of pulmonary oedema or a coronary event, occurring in the absence of hypotension, and characterized by hepatic damage and renal functional impairment. The aim of this study was to describe the features, circumstances of appearance, and response to therapy of CAHIRI.

Twenty-five consecutive patients with CAHIRI were observed prospectively. The onset of CAHIRI was characterized by an abrupt increase of alanine aminotransferase (median peak 988 IU/Dl), aspartate aminotransferase (median peak 528 IU/Dl) and serum creatinine, with blood urea nitrogen/creatinine ratio > 15. Treated with conventional medications the course of CAHIRI was fatal in 4/4 cases. Twenty-one patients were treated with the splanchnic vasodilator dopamine 2.5 µg/min/kg. The hepatic and renal tests peaked on days 2–3 and subsequently improved, however, an unexpected deterioration of cardiac function occurred in 15 cases, mostly on days 3–5, and was the chief cause of death in 52 % of the dopamine treated patients.

CAHIRI is a severe but potentially reversible complication of congestive heart failure, that should be promptly recognized and treated. The early improvement of symptoms and laboratory alterations may be misleading since a second bout of heart failure often ensues, precipitating the patient's death. Improvement of the outcome of CAHIRI might be dependent on the better understanding of the pathogenesis of this second bout of heart failure, on haemodynamic monitoring during the five-day vulnerable period, and on introduction of new therapies. *J Clin Basic Cardiol 2000; 3: 35–8.*

Key words: heart failure, ischaemic hepatitis, dopamine

Abnormalities in liver function tests have been noted frequently in patients with chronic congestive heart failure. They are generally mild and not associated with clinically apparent hepatic disease [1, 2]. An occasional patient with heart failure, however, may demonstrate striking evidence of hepatic necrosis, sometimes exhibiting hepatic coma, and often bringing about the patient's death. While vaguely resembling acute viral hepatitis, this condition termed 'ischaemic hepatitis' has quite distinct clinical laboratory and histologic features [3–5]. We have described a variant of ischaemic hepatitis [6, 7], characterized by combined cardiogenic hepatic injury and renal impairment. This complication occurs in patients with severe chronic congestive heart failure, following an episode of pulmonary oedema or an acute coronary event and in the absence of arterial hypotension. It differs from isolated ischaemic hepatitis and isolated renal damage by the combined visceral involvement and from 'shock liver' [8] and 'shock kidney' [9] by apparently not being preceded by hypotension. In the present analysis we extended the preliminary observations [6, 7] on cardiogenic hepatic injury and renal impairment (CAHIRI) to describe the circumstances of appearance, the clinical and laboratory features, and the response to therapy of the disorder.

Methods

The diagnosis of CAHIRI was established when the following criteria were met:

1. Cardiogenic pulmonary oedema, an acute coronary event [10], or both preceded the alterations in the hepatic and renal tests by up to 48 hours
2. Increase of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), or both to 500 IU/Dl or more
3. Increase of serum creatinine by 0.5 mg/Dl or more, with concomitant serum BUN/creatinine ratio of 15 or more
4. No overt arterial hypotension, ie systolic blood pressure below 90 mmHg or decrease of the systolic blood pressure by 30 mmHg or more of baseline.

Included in this study were 25 consecutive patients with CAHIRI diagnosed and treated at the Department of Internal Medicine A during the study period 1981–1995 and followed prospectively. Excluded were alcoholics, patients with viral or drug induced hepatitis [11], or infection on admission. The work-up included a detailed history and physical examination, electrocardiogram, chest X-ray, echocardiography or radionuclide ventriculography. The following parameters were regularly monitored: arterial blood pressure by sphygmomanometry, urinary output and electrocardiogram. Daily hepatic and renal functions, blood gases, as well as chest X-ray examinations were performed. Invasive monitoring of the systemic arterial pressure, pulmonary artery and capillary wedge pressure, cardiac output, systemic and pulmonary resistances was done in selected patients.

The following clinical data were studied: sex and age, rates of chronic congestive heart failure, chronic liver disease, chronic obstructive lung disease, and chronic renal disease, types of triggering events and the lag-time to CAHIRI. The following laboratory data were analyzed: parameters of hepatocellular damage – aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), parameters of renal function – serum creatinine and blood urea nitrogen (BUN), and parameters of disseminated intravascular coagulation. The upper limit of the normal ranges in our laboratory are AST and ALT 40 IU/Dl, LDH 200 IU/Dl, creatinine 1.2 mg/Dl, BUN 20 mg/Dl, potassium 5.5 mEq/L, partial thromboplastin time 36 seconds. The lower limit of the normal ranges are serum fibrinogen 300 mg/Dl, platelet count 140,000/mm³, and prothrombin index 70 %. Serologic tests for hepatitis included hepatitis B surface antigen, anti-hepatitis B core antibodies and anti-hepatitis C virus antibodies. The tests were performed with commercial kits from Abbott Laboratories.

The first 4 patients were treated with diuretics, preload and afterload-reducing agents, and other medications taken prior to the acute episode. Digoxin was withheld. The subsequent 21 patients to develop CAHIRI received low-dose dopamine

Received June 15th, 1999; accepted August 11th, 1999.

From the Departments of ¹Internal Medicine, ²Pathology and ³Cardiology, the Bnai Zion Medical Center, and the Bruce Rappaport Faculty of Medicine, Technion Israel Institute of Technology, Haifa, Israel.

Correspondence to: Jochanan E. Naschitz, MD, Department of Internal Medicine A, Bnai Zion Medical Center, P.O. Box 4940, 31048 Haifa, Israel

treatment [12] in addition to prior medications. Dopamine intravenously at a rate of 2.5 µg/min/kg body weight was started immediately after the diagnosis of CAHIRI and was administered for 3 to 5 days.

In patients with a favorable outcome, the time for the laboratory abnormalities to return to baseline levels and duration of hospital stay were established. The time and causes of in-hospital mortality were analyzed. Liver needle necropsy was performed in 5 cases. Survivors of a first episode of CAHIRI were followed at the outpatient clinic: cumulative survival of the patients was estimated by the Kaplan-Meier method [13].

Results

Twenty-five episodes of CAHIRI were diagnosed during the 15-year study period at the Department of Internal Medicine among 1308 episodes of cardiogenic pulmonary oedema (in 327 patients) and 2487 acute coronary events (in 1363 patients). There were 18 males and 7 females and their ages ranged from 63 to 94 years (median 78 years). Twenty-three patients had been previously diagnosed and treated for chronic congestive heart failure, 21 of whom belonged to NYHA classes III and IV. In 2 cases there was no previously recognized heart failure. The etiologies of chronic congestive heart failure included ischaemic heart disease (n = 11), diabetes mellitus (n = 1); valvulopathies (n = 1), or combinations of the above (n = 12). In all patients, cardiomegaly was present on chest X-rays, and left ventricular systolic dysfunction on echocardiography. One or more episodes of prior pulmonary oedema, not followed by CAHIRI, were on record for 16 patients. Among preexistent diseases, chronic liver disease was noticed in 2 patients (both tested positive for hepatitis B surface antigen and had 2- to 3-fold increase in ALT and AST for several years), chronic obstructive pulmonary disease in 10 patients and mild chronic renal failure in 7 patients. Medications on the verge of occurrence of the CAHIRI included digoxin diuretics, as well as

preload and afterload-reducing agents. Three or more of the latter medications were given to 14 patients. Pulmonary oedema (in 21 patients) and an acute coronary event (in 3 patients) preceded CAHIRI by 3 to 48 hours (median 25 hours). No precipitating event could be identified in one patient (Table 1). Pulmonary oedema required positive-pressure ventilation in 2 patients.

The clinical picture of CAHIRI included weakness, apathy and loss of appetite in all patients. Mental confusion was noticed in 5, slight jaundice in 12, anuria or oliguria at onset of CAHIRI in 8 patients. None developed flapping tremor or coma. The main laboratory abnormalities are shown in Table 2. These abnormalities reached their peak 1 to 3 days after onset of CAHIRI (Figure 1). Prolonged prothrombin time was observed in 16 patients. In 7 patients, one or several additional coagulation tests were abnormal: prolonged partial thromboplastin time, low fibrinogen levels, elevated fibrin-fibrinogen split products, thrombocytopenia, positive D-dimer test. None of the patients had blood sugar values less than 60 mg/dl.

The first 4 patients were not treated with dopamine. All died 2-4 days after the onset of CAHIRI. Twenty-one subsequent patients, received low-dose dopamine therapy and 10 patients recovered. Improvement of heart failure and ischaemic symptoms were noticed in 22 patients within 4 to 24 hours from the triggering event; heart failure did not reverse in 3 patients. Improvement of the hepatic and renal tests began 1 to 10 days after the triggering event. In 15 patients, a second

Table 1. Clinical setting of CAHIRI

Patient characteristics	No. of cases
Total cases	25
Sex distribution (males : females)	18 : 7
Age (years; median and range)	78 (63 to 94)
Chronic congestive heart failure (NYHA class)	I: 22, II: 2; III: 8; IV: 13
Chronic liver disease	2
Chronic obstructive lung disease	10
Chronic renal disease	7
Antecedent acute coronary event*	3
Antecedent acute pulmonary oedema*	21

* 48 hours or less before CAHIRI was diagnosed

Table 2. Laboratory abnormalities during the course of CAHIRI (peak values)

Variables	Peak value median (range)	Days to peak value* median (range)
AST (U/Dl)	988 (399-7300)	2 (1-10)
ALT (U/Dl)	528 (159-6540)	2 (1-10)
LDH (U/Dl)	772 (361-6440)	3 (1-10)
Prothrombin time (%)	39 (21-92)	1 (1-3)
Serum potassium (mEq/L)	4.7 (3.1-8.0)	1 (1-3)
Serum creatinine (mg/Dl)	2.4 (1.5-6.2)	2 (1-10)
BUN (mg/Dl)	48 (16-61)	3 (1-10)

* From precipitating event to peak value

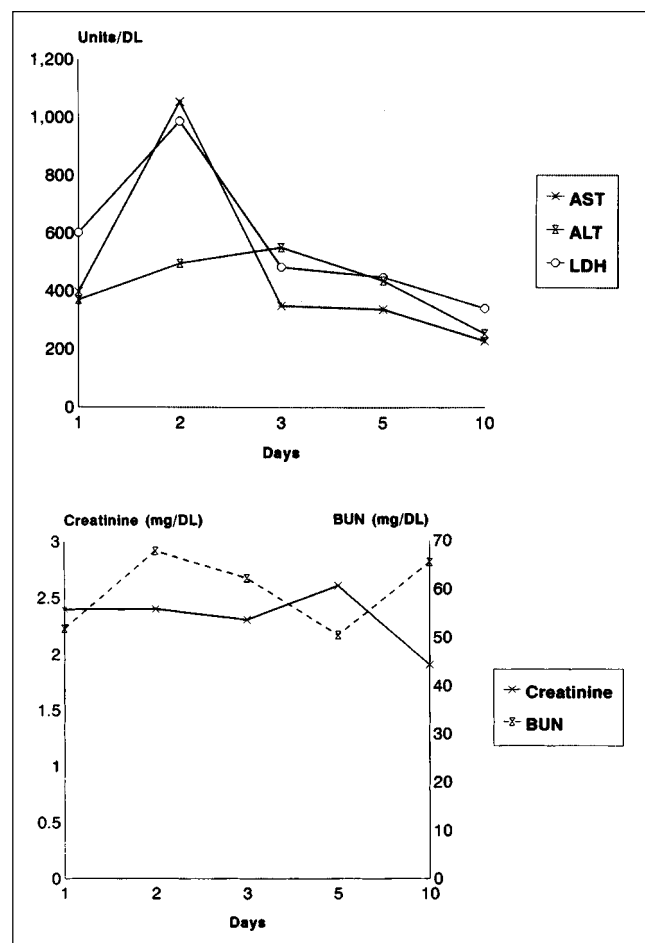


Figure 1. Time-course of liver and kidney function tests during CAHIRI

deterioration of heart failure occurred on days 2 to 5 (median 4 days) after the initial triggering event.

In survivors, the time to recovery of the laboratory abnormalities was 4–90 days (median 4 days) (Tables 2 and 3, Figure 1). The time to death following CAHIRI was 1–23 days (median 4 days) (Table 3 and Figure 2). The causes of death in dopamine-treated subjects were intractable heart failure ($n = 2$), cardiogenic shock ($n = 8$), and sepsis ($n = 1$). No patient developed hepatic coma or severe renal failure necessitating dialysis. The histological picture of the liver in 5 patients in whom liver needle necropsy was obtained showed centrilobar necrosis.

Among the 10 survivors, 3 patients are alive at 200, 360, and 490 days following CAHIRI. 7 patients died, at 180–722 days following CAHIRI (median 420 days). The causes of late death were congestive heart failure in 4, cerebrovascular accident in 1, and myocardial infarction in 2 patients. During outpatient follow-up, 7 episodes of pulmonary oedema occurred in 5 patients and were treated with low-dose dopamine; none developed CAHIRI.

Table 3. Follow-up data of patients with CAHIRI

Parameter	Days	
	Median	Range
Lag-time from triggering event to diagnosis of CAHIRI ($n = 23$)*	1	3 hours–2 days
Time to second-bout heart failure ($n = 15$)*	4	2–5 days
Time to recovery of laboratory abnormalities** ($n = 10$)	4	4–90 days
Time to hospital death ($n = 15$)	4	1–23 days

* Triggering event could not be determined in 2 cases.
** Return to baseline levels

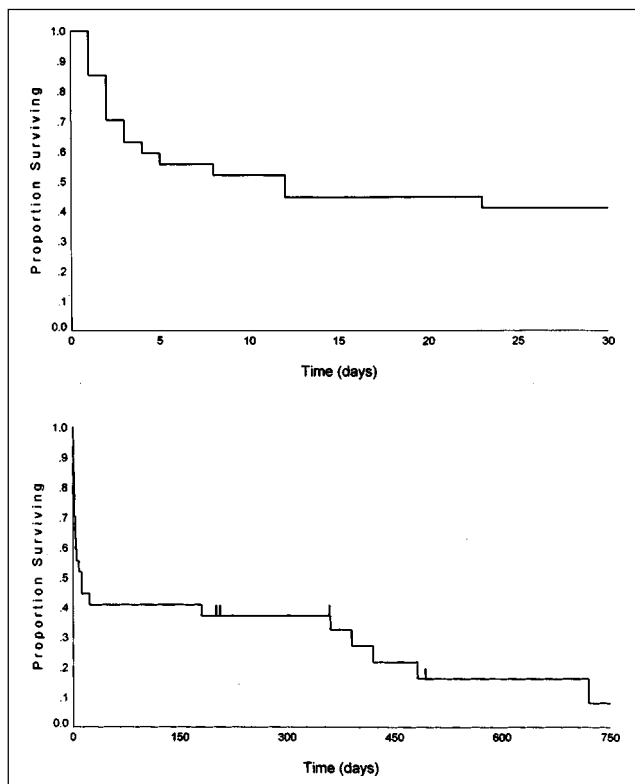


Figure 2. Overall survival following CAHIRI illustrated with the aid of Kaplan-Meier curves. In surviving patients, the time elapsed from CAHIRI to the time of writing is figured by vertical marks.

Discussion

Among the complications of congestive heart failure, CAHIRI has been only occasionally mentioned [14, 15]. Nevertheless, CAHIRI is not exceedingly rare, since we observed 25 cases during a 15-year period. Hepatic injury in CAHIRI is consistent with 'ischaemic hepatitis' [1, 4]. The diagnosis of ischaemic hepatitis is stated when, in the appropriate context, a sharp increase in serum aminotransferase activity between 10 and 20 times the upper limit of normal occurs and is followed by a more than 50% decrease within 72 hours. Such time course of the biochemical alterations excludes the possibility of alcoholic, viral or drug-induced hepatitis [5]. In contradistinction to the organic hepatic injury, renal impairment in CAHIRI was of functional nature. We named the renal counterpart of the syndrome 'renal impairment' in order to underscore its functional nature. Such type of renal functional derangement is noticed under circumstances reducing the effective circulatory volume or when local vasomotor alterations diminish the glomerular capillary pressure [9].

Hepatic injury and prerenal failure occurred in close proximity to cardiac decompensation (21 patients) or to a coronary event (3 patients). On the basis of the temporal relationship with a precipitating cardiac event, the similarity to well-recognized cardiogenic endorgan damage, and in the absence of other etiologies, we submit that the syndrome is caused by heart failure. As in isolated ischaemic hepatitis [4] and isolated cardiogenic renal failure [9], CAHIRI can be regarded as a form fruste of cardiogenic shock. While the cardiac etiology is obvious, the appearance of the syndrome is, nevertheless, unpredictable. Among patients who had numerous episodes of pulmonary oedema, the duration and severity of pulmonary oedema was not related to the subsequent occurrence of CAHIRI. In a previous study we compared patients who had CAHIRI with matched controls in a search for clinical and laboratory markers that could predict the occurrence of CAHIRI. Neither antecedent hepatic or renal derangement nor suspected triggering factors such as medications, hypovolaemia, hyponatraemia, and intercurrent infections were more prevalent in the CAHIRI group [7].

CAHIRI is distinct from other disorders involving both kidneys and liver such as overt cardiogenic shock [8], hepato-renal syndrome in cirrhosis or acute viral hepatitis [14], multiple system organ failure syndrome [16], and the systemic inflammatory response syndrome [17].

Considerations as to the pathophysiology of CAHIRI are based on clinical data and analogies to related disorders.

- CAHIRI was noticed almost exclusively in patients with chronic but not in acute heart failure. Among the compensatory responses evoked by chronic heart failure, their excessive activation may have deleterious consequences. Such are activation of the sympathetic nervous system, renin-angiotensin-aldosterone system, and increased renal formation of the vasoconstrictor prostaglandins thromboxane A₂ and prostaglandin F_{2α}, which may lead to uncontrolled vasoconstriction and may predispose to tissue ischaemia [18–21].

- Pharmacological agents interfering with adaptive mechanisms in the hepatic and renal circulations: Angiotensin-converting enzyme inhibitors by interference with the local adaptive mechanisms may decrease the hepatic blood flow in patients with congestive heart failure [22, 23]; captopril, calcium antagonists, furosemide, and nonsteroidal anti-inflammatory agents may have deleterious effects on the ischaemic kidney [24]. Continuous positive-pressure ventilation may cause significant decrease in hepatic blood flow, leading to hepatic injury [25].

• Acute hypoxaemia: Acute hypoxaemia has been described in some circumstances as the exclusive cause of ischaemic hepatitis [26] and acute hypoxaemia developing during pulmonary oedema may, obviously, aggravate preexisting hepatic hypoxia caused by chronic circulatory impairment.

• Reperfusion injury: Much of the hepatic damage develops during ischaemia, however, reperfusion may cause further damage to the liver by afflux of oxygen derived free radicals [27].

• Tumor necrosis factor: Released from macrophages in underperfused tissues, tumor necrosis factor depresses myocardial contractility and can be one of the factors that perpetuate heart failure [28] or cause the second bout of heart failure in CAHIRI.

• Substances of intestinal origin: The pathogenic effects of toxic, infectious, peptic and inflammatory substances of intestinal origin may lead to 'multiple system organ failure'. The latter manifests one or several of the following: decreased myocardial contractility, decreased renal function, and pulmonary dysfunction [16, 29].

Mortality in CAHIRI was usually related to a second-phase deterioration of heart failure that occurred mostly on days 2 to 5, in spite of the fast initial amelioration of clinical symptoms and laboratory abnormalities. The immediate trigger for the second-phase deterioration of heart failure is unknown. Improvement of the outcome of CAHIRI might be dependent on the better understanding of the pathogenesis of this second bout of heart failure and on additional therapeutic modalities.

There are limitations to this study. First our patients were all from a single referral clinic, and thus the results might not be generalizable to other clinical settings. Second, the exact time relationships of systemic haemodynamics and visceral ischaemia could not be specified. Future studies comprising haemodynamic monitoring and sequential determination of circulating cytokine levels might shed light on the pathogenesis of the second bout of heart failure in CAHIRI. Third, our study, which extends over a 15 year period, could not examine the effect of some novel therapies such as L-arginine to increase nitric oxide production [30], acetylcysteine to improve microcirculation in the liver [31], antioxidants [24, 28], antibiotics [19], and intraluminal oxygenation of the gut [32]. Establishment of a prospective multicenter trial for the treatment of CAHIRI is well-timed.

In conclusion, CAHIRI is a severe but potentially reversible complication of congestive heart failure that should be promptly recognized and treated. The early improvement of symptoms and laboratory alterations may be misleading since a second bout of heart failure often ensues, precipitating the patient's death. Improvement of the outcome of CAHIRI might be dependent on the better understanding of the pathogenesis of this second bout of heart failure, on haemodynamic monitoring during the five-day vulnerable period, and on introduction of new therapies.

References

- Sherlock S. The liver in circulatory failure. In: Schiff L, Schiff ER (eds). Diseases of the liver. Seventh Edition. J.B. Lippincott Company, Philadelphia, 1993; 1431-7.
- Kubo C, Walter BA, John DHA, Clark M, Cody RJ. Liver function abnormalities in chronic heart failure. Influence of systemic hemodynamics. Arch Intern Med 1987; 147: 1227-30.
- Gibson PP, Dudley FJ. Ischemic hepatitis: clinical features, diagnosis and prognosis. Aust NZ J Med 1984; 14: 822-5.
- Fuchs S, Bogomolski-Yahalom V, Paltiel O, Ackerman Z. Ischemic hepatitis. Clinical and laboratory observations in 34 patients. J Clin Gastroenterol 1998; 26: 183-6.
- Pauwels A, Levy VG. Ischemic hepatitis in cirrhosis: not so rare, not always lethal. J Clin Gastroenterol 1993; 17: 88-9.
- Naschitz JE, Yeshurun D. Compensated cardiogenic shock: a subset with damage limited to liver and kidney. The possible salutary effect of low-dose dopamine. Cardiology 1986; 74: 212-8.
- Naschitz JE, Yeshurun D, Shahar J. Cardiogenic hepatorenal syndrome. Angiology 1990; 41: 893-900.
- Birgens HS, Henriksen J, Matzen P, Poulsen H. The shock liver. Acta Med Scand 1978; 204: 417-21.
- Brady HR, Singer GG. Acute renal failure. Lancet 1995; 346: 1533-40.
- Theroux P, Waters D. Diagnosis and management of patients with unstable angina. In: Schlant RC, Alexander RW, O'Rourke RA, Sonnenblick EH (eds). The heart, arteries and veins. McGraw-Hill, New York, 1994; 1084.
- Zimmerman NH. Hepatotoxicity: The adverse effects of drugs and other chemicals on the liver. Appleton Century Crofts, New York, 1978; 55.
- Levy DK, Schwartz DM, Frishman WH, Schwartz ML, LeJemtel TH. Ischemic hepatitis in a patient with congestive cardiomyopathy: an innovative approach to therapy using intravenous dobutamine. J Clin Pharmacol 1994; 34: 270-2.
- Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. J Am Stat Assoc 1958; 53: 457-81.
- Conn HO. A rational approach to the hepatorenal syndrome. Gastroenterology 1973; 65: 321-40.
- Clinicopathologic conference. Congenital heart disease in a male adult. Am J Med 1981; 70: 1107-12.
- Carrico CJ. The elusive pathophysiology of the multiple organ failure syndrome. Ann Surg 1993; 218: 109-10.
- Rangel-Frausto SM, Pittet D, Costigan M, Hwang T, Davis CS, Wenzel RP. The natural history of the systemic inflammatory response syndrome (SIRS). A prospective study. JAMA 1995; 273: 117-23.
- Bailey GB, Bulkey GB, Hamilton SR. Protection of the small intestine from nonocclusive mesenteric ischemia injury due to cardiogenic shock. Am J Surg 1987; 153: 108-16.
- Kon V, Yared A, Ichikawa I. Role of renal sympathetic nerves in mediating hypoperfusion of renal cortical microcirculation in experimental congestive heart failure and acute extracellular fluid volume depletion. J Clin Invest 1985; 76: 1913-20.
- Ichikawa I, Pfeffer JM, Pfeffer MA, Hostetter TH, Brenner BM. Role of angiotensin II in the altered renal function of congestive heart failure. Circ Res 1984; 55: 669-75.
- McCarthy Pastores S, Katz DP, Kvetan V. Splanchnic ischemia and gut mucosal injury in sepsis and the multiple organ dysfunction syndrome. Am J Gastroenterol 1996; 91: 1697-1710.
- Ontell SJ, Makowka L, Trager J, Mazzaferro V, Ove P, Starzl TE. Pharmacologic modulation of experimental posts ischemic hepatic function. Ann Surg 1989; 209: 209-10.
- Creager MA, Halperin JL, Bernard DB, Faxon DP, Melidossian CD, Gavras H, Ryan TJ. Acute regional circulatory and renal hemodynamic effects of converting-enzyme inhibition in patients with congestive heart failure. Circulation 1981; 64: 483-9.
- Badr KF, Ikawa J. Prerenal failure: a deleterious shift from renal compensation to decompensation. N Engl J Med 1988; 319: 623-8.
- Bonnet F, Richard C, Glaser P, Lafay M, Guesde R. Changes in hepatic flow induced by continuous positive pressure ventilation in critically ill patients. Crit Care Med 1982; 10: 703-5.
- Mathurin P, Durand F, Ganne N, Mollo J-L, Lebrec D, Degott S, Benhamou J-P, Bernuau J. Ischemic hepatitis due to obstructive sleep apnea. Gastroenterology 1995; 109: 1682-4.
- Younes N, Wagner H, Strubelt O. Enhancement of acute ethanol hepatotoxicity under conditions of low oxygen supply and ischemia/reperfusion. The role of oxygen radicals. Biochem Pharmacol 1989; 38: 3573-81.
- Packer M. Is tumor necrosis factor an important neurohormonal mechanism in chronic heart failure? Circulation 1995; 92: 1379-82.
- Reilly PM, Bulkley GB. Vasoactive mediators of splanchnic perfusion. Crit Care Med 1993; 21: S55-S68.
- Koifman B, Wollman Y, Bogomolny N, Chernichowsky T, Finkelstein A, Peer G, Scherez J, Blum M, Laniado S, Iaina A, Keren G. Improvement of cardiac performance by intravenous infusion of L-arginine in patients with moderate congestive heart failure. JACC 1995; 26: 1251-6.
- Devlin J, Ellis E, McPeake J, Wendon J, Williams R. N-acetyl-cysteine improves ICG clearance in addition to systemic hemodynamics during severe hepatic (graft) dysfunction. Hepatology 1994; 20: 123A.
- Haglund U. Therapeutic potential of intraluminal oxygenation. Crit Care Med 1993; 21: S69-S71.

Mitteilungen aus der Redaktion

Besuchen Sie unsere zeitschriftenübergreifende Datenbank

[Bilddatenbank](#)

[Artikeldatenbank](#)

[Fallberichte](#)

e-Journal-Abo

Beziehen Sie die elektronischen Ausgaben dieser Zeitschrift hier.

Die Lieferung umfasst 4–5 Ausgaben pro Jahr zzgl. allfälliger Sonderhefte.

Unsere e-Journale stehen als PDF-Datei zur Verfügung und sind auf den meisten der marktüblichen e-Book-Readern, Tablets sowie auf iPad funktionsfähig.

[Bestellung e-Journal-Abo](#)

Haftungsausschluss

Die in unseren Webseiten publizierten Informationen richten sich **ausschließlich an geprüfte und autorisierte medizinische Berufsgruppen** und entbinden nicht von der ärztlichen Sorgfaltspflicht sowie von einer ausführlichen Patientenaufklärung über therapeutische Optionen und deren Wirkungen bzw. Nebenwirkungen. Die entsprechenden Angaben werden von den Autoren mit der größten Sorgfalt recherchiert und zusammengestellt. Die angegebenen Dosierungen sind im Einzelfall anhand der Fachinformationen zu überprüfen. Weder die Autoren, noch die tragenden Gesellschaften noch der Verlag übernehmen irgendwelche Haftungsansprüche.

Bitte beachten Sie auch diese Seiten:

[Impressum](#)

[Disclaimers & Copyright](#)

[Datenschutzerklärung](#)