Jak používám dobutamin a levosimendan

Robert Janda
Jednotka intenzivní péče
OARIM Karlovy Vary

Karlovarská krajská nemocnice

Přesněji: kdy a jak…

- **V resuscitaci šoku**
- **Když chci zvýšit tkáňovou perfuzi (flow)**
- **Vždy za komplexní monitorace v anamnestickém a klinickém kontextu**
- **Dle doporučení**
- **Po optimalizaci perfuze tekutinami a NOR**
- **S myšlenkou na další optimalizaci VO2/ DO2**
- **Málo…, levosimendan minimálně**

Podání inotropika v šoku

Intensive Care Med (2014) 40:1795–1815
DOI 10.1007/s00134-014-3525-z

CONFERENCE REPORTS AND EXPERT PANEL

Maurizio Cecconi
Daniel De Backer
Massimo Antonelli
Richard Beale
Jan Bakker
Christoph Hofer
Roman Jaeschke
Alexandre Mebazaa
Michael R. Pinsky
Jean Louis Teboul
Jean Louis Vincent
Andrew Rhodes

Consensus on circulatory shock and hemodynamic monitoring. Task force of the European Society of Intensive Care Medicine

Definition, pathophysiology, features and epidemiology of shock

Definition

Shock is best defined as a life-threatening, generalized form of acute circulatory failure associated with inadequate oxygen utilization by the cells. It is a state in which the circulation is unable to deliver sufficient oxygen to meet the demands of the tissues, resulting in cellular dysfunction. The result is cellular dysoxia, i.e. the loss of the physiological independence between oxygen delivery and oxygen consumption, associated with increased lactate levels. Some clinical symptoms suggest an impaired microcirculation, including mottled skin, acrocyanosis, slow capillary refill time and an increased central-to-toe temperature gradient.

- Fyziologický vztah VO2 a DO2 je narušen.
- DO2=CaO2 x CO,..(význam SaO2, Hb, preload, afterload, kontraktilita, rytmus, HR).
- **Po předchozí „optimální“ resuscitaci tekutinou a NOR a po event. „kontrole“ nároků na O2 (T, WOB) jsou známky možné hypoperfuze/ hypoxie/ dysoxie. Chci zvýšit flow - uvažuji o inotropiku.**
- Řídím se perfuzí, ne hodnotou DO2 („supranormální flow“ může škodit – Heyes, NEJM 1994).

Síla doporučení pro intropika

Consensus on circulatory shock and hemodynamic monitoring. Task force of the European Society of Intensive Care Medicine → Level 2, QoE low (C)

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016 → Weak rec., QoE low (C)

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure → II b, QoE low (C)

Méně katecholaminů v šoku?

Diskuse o negativech: CNS, imunita, růst bakterií, metabolismus, tkáňová perfuse, myokard…
Málo klinických dat:

Abraham WT, Adams KF, Fonarow GC et al (2005) In-hospital mortality in patients with acute decompensated heart failure requiring intravenous vasoactive medications: an analysis from the Acute Decompensated Heart Failure National Registry (ADHERE). J Am Coll Cardiol 46:57–64

Brown SM, Lanspa MJ, Jones JP et al (2013) Survival after shock requiring high-dose vasopressor therapy. Chest 143:664–671

Leibovici L, Gafter-Gvili A, Paul M et al (2007) Relative tachycardia in patients with sepsis: an independent risk factor for mortality. QJM 100:629–634

Boldt J, Menges T, Kuhn D et al (1995) Alterations in circulating vasoactive substances in the critically ill: a comparison between survivors and non-survivors. Intensive Care Med 21:218–225

Levosimendan jako alternativa k dobutaminu v sepsi ? LeoPARD.

Levosimendan for the Prevention of Acute Organ Dysfunction in Sepsis

RESULTS

The trial recruited 516 patients; 259 were assigned to receive levosimendan and 257 to receive placebo. There was no significant difference in the mean (±SD) SOFA score between the levosimendan group and the placebo group (6.68±3.96 vs. 6.06±3.89; mean difference, 0.61; 95% confidence interval [CI], −0.07 to 1.29; P=0.053). Mortality at 28 days was 34.5% in the levosimendan group and 30.9% in the placebo group (absolute difference, 3.6 percentage points; 95% CI, −4.5 to 11.7; P=0.43). Among patients requiring ventilation at baseline, those in the levosimendan group were less likely than those in the placebo group to be successfully weaned from mechanical ventilation over the period of 28 days (hazard ratio, 0.77; 95% CI, 0.60 to 0.97; P=0.03). More patients in the levosimendan group than in the placebo group had supraventricular tachyarrhythmia (3.1% vs. 0.4%; absolute difference, 2.7 percentage points; 95% CI, 0.1 to 5.3; P=0.04).

N ENGL J MED 375;17 NEJM.ORG OCTOBER 27, 2016

V kardiochirurgii? LEVO-CTS, CHEETAH trials
N Engl J Med 376:2076-2078,
May 25, 2017

Dobutamin nebo levosimendan?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Levosimendan for the Prevention of Acute Organ Dysfunction in Sepsis

N ENGL J MED 375;17 NEJM.ORG OCTOBER 27, 2016

LEVO-CTS, CHEETAH trials
N Engl J Med 376:2076-2078,
May 25, 2017

Levosimendan vs Dobutamine for Patients With Acute Decompensated Heart Failure
The SURVIVE Randomized Trial

JAMA, May 2, 2007—Vol 297, No. 17

ELSEVIER

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.jccjournal.org

Sepsis

Levosimendan reduces mortality in patients with severe sepsis and septic shock: A meta-analysis of randomized trials☆,☆☆

A. Zangrillo et al. / Journal of Critical Care 30 (2015) 908–913

ELSEVIER

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Review

Levosimendan meta-analyses: Is there a pattern in the effect on mortality?

P. Pollesello et al. / International Journal of Cardiology 209 (2016) 77–83

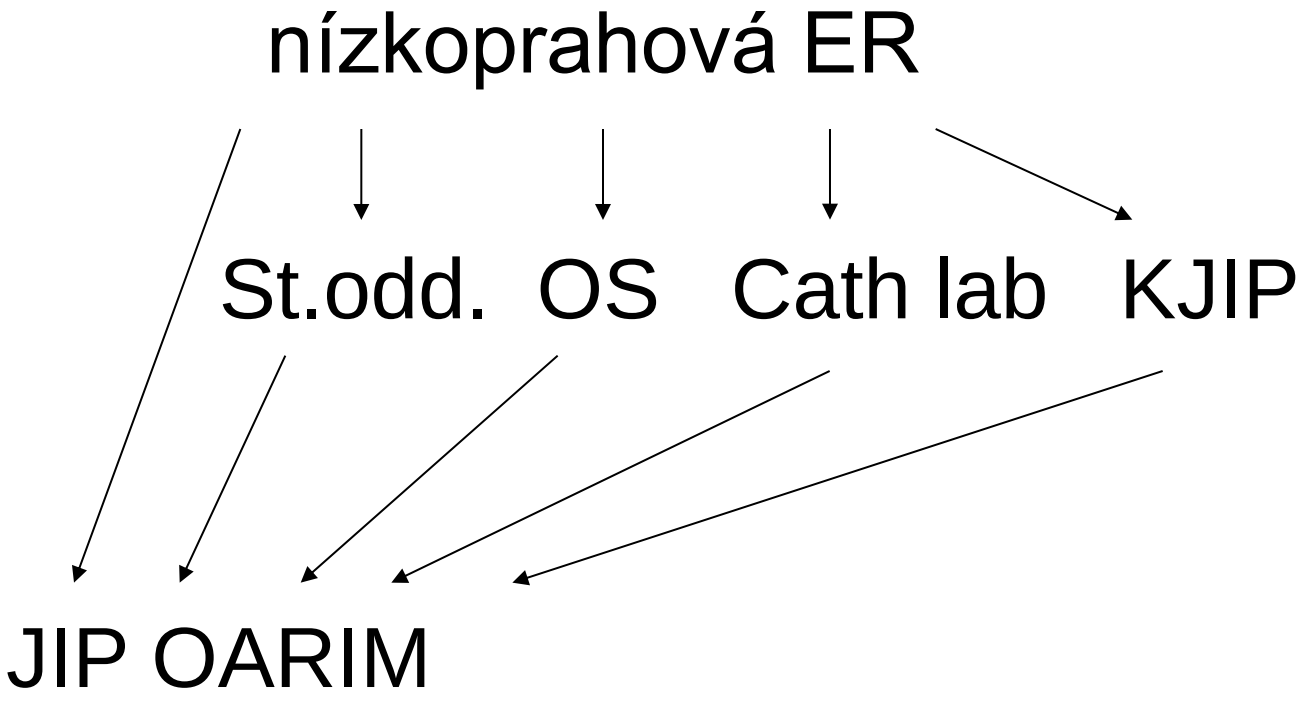
Levosimendan ve všeobecné IP užíváme minimálně.

Monitorace v KV před a po nasazení inotropika

- Monitorace klinického stavu, hemodynamiky, markerů tkáňové perfuze a (buněčné) oxygenace v průběhu dg. a terapie šoku.
- Monitorace efektu tekutin a vasopresorů, nalezení správného okamžiku indikace k podání inotropik. **Optimalizace další terapie tekutinami, vasopresory a inotropiky s důrazem na její možné vedlejší účinky. Lék, který není indikován je kontraindikován.**
- Cílem je zajištění tkáňové normoxie, resp.odstranění tkáňové hypoxie a prevence vzniku tkáňové dysoxie. Zabránit rozvoji kyslíkového dluhu, buněčného poškození, orgánového selhání a smrti (**Rivers et al**, Current Opinion in Critical Care 2015).

Pohyb kriticky nemocných v KKN

Menší KN (500 lůžek), Kardiocentrum bez KCH



Monitorace v průběhu resuscitace nemocného v hypotenzi/ šoku v KV

- Na ER/ JIP : anamnéza…fyzikální vyšetření (pohled/ pohmat/ poslech)…STK + GCS + RR = q SOFA (ER/St.O). SpO2…EKG (ST/ rytmus/ HR)…T…**TTE**. Kanylace tepny – MAP + **laktát** + SaO2 + Hb. Diuréza. Po ETI…odhad SPV…VCCd. MAP po terapii tekutinou – indikace k NOR?

- + Na JIP/ OS : kanylace VS/ VJI: **laktát, SaO2/ ScvO2…(delta PCO2?) …TTE (LVEF, VCCd) + LiDCO.**

Laktát jako základní ukazatel

Early Lactate-Guided Therapy in Intensive Care Unit Patients
A Multicenter, Open-Label, Randomized Controlled Trial

AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE VOL 182 201(

Lactate Clearance vs Central Venous Oxygen Saturation as Goals of Early Sepsis Therapy
A Randomized Clinical Trial

JAMA. 2010;303(8):739-746

Clinical use of lactate monitoring in critically ill patients

Bakker *et al. Annals of Intensive Care* 2013, **3**:12

ScvO2: EGDT(Rivers) + ProMISe, ARISE, ProCESS

- 3 nové studie „nepotvrdily“ užitečnost Riversova protokolu s užitím ScvO2…
- Zjistily, že protokol z roku 2001 nefunguje v roce 2014/ 2015…
- Diskuse: Rivers et al. (Curr Opin Crit Care 2015), Nguyen et al. (Critical Care 2016), D. De Backer a J.L.Vincent (Intensive Care Med 2016) x Angus et al. (Intensive Care Med 2015), PRISM investigators (NEJM 2017)
- **Filozofie užití ScvO2 v monitoraci a léčbě nejspíše byla a je správná. Konkrétní onemocnění může probíhat ve fázích s různým „fenotypem“ a s jemu odpovídající mortalitou…**
- **V indikaci inotropika užívám kombinaci markerů hemodynamiky (LiDCO) + uvažuji také hodnoty laktátu a ScvO2 a…**

	Refractory hypotension (%)	Lactate >4 mmol/l (%)	$ScvO_2$ (%)	Lactate (mmol/l)	Hospital mortality (%)
EGDT [5][a]	51.1–54.6	79–80	48.6–49.2	6.9–7.7	30.5–46.5
Holst *et al.* [58••]	All	n/a	68–69	2.4–2.7	43–45
ProCESS [7••][b]	53.5–55.6	59.0–60.7	71	4.8–5.0	18.2–21.0
ARISE [9••][b]	69.8–70.0	46.3–46.5	72.7	4.2–4.4	14.5–15.7
ProMISE [8••][b]	54.1–55.6	63.7–65.4	70.1	5.1–5.2	24.0–25.0
Jones *et al.* [59][a]	74–82	39	74	3.9–4.2	16.7–22.0

Stage	Haemodynamic Derangements	Lactate	SvO_2/$ScvO_2$	MAP	Mortality (%)	Treatment and Comments
A	Hypovolaemia, vasodilatation, myocardial suppression, increased metabolic demands	Normal	↓	↓	15% (12), 23% (29)	Volume, vasopressors, correct anaemia, inotropic therapy, mechanical ventilation
		↑		Normal	21% (21), 24.9% (27), 35.2% (28) (cryptic shock)	
B	Resuscitated, compensated and vasodilatory	Normal - ↑	Normal	↓	19.0% (21), 20% (56)	Hyperdynamic, vasopressors, low-dose corticosteroids
				Normal	7.7% (55), 11.8% (61), 21% (48)	
C	Continued DO_2 dependency, increased metabolic demands	↑	↓	↓	37.9% (61), 40% (48), 42.9% (55), 48% (27), 51% (12)	Decrease VO_2 and further augmentation of DO_2
D	Microcirculatory or OER defections and impairment of VO_2 Decreased VO_2 (dysoxic)	↑	↑	↓	34% (48), 40% (12), 41.7% (61), 52.3% (26), 60.3% (28)	Microcirculatory rescue, source control

Rivers et al **Curr Opin Crit Care** 2015, 21:381–387

PvCO2 - PaCO2 jako vodítko pro manipulaci s DO2?

Lamia B, Monnet X, Teboul JL. Meaning of arterio-venous PCO2 difference in circulatory shock. *Minerva Anestesiol* 2006; **72**: 597-604 [PMID: 16682934]

Intensive Care Med (2008) 34:2218–2225
DOI 10.1007/s00134-008-1199-0

ORIGINAL

Fabrice Vallée
Benoit Vallet
Olivier Mathe
Jacqueline Parraguette
Arnaud Mari
Stein Silva
Kamran Samii
Olivier Fourcade
Michèle Genestal

Central venous-to-arterial carbon dioxide difference: an additional target for goal-directed therapy in septic shock?

Intensive Care Med (2013) 39:1034–1039
DOI 10.1007/s00134-013-2888-x

ORIGINAL

Paul A. van Beest
Mariska C. Lont
Nicole D. Holman
Bert Loef
Michaël A. Kuiper
E. Christiaan Boerma

Central venous-arterial pCO_2 difference as a tool in resuscitation of septic patients

Intensive Care Med (2013) 39:1653–1655
DOI 10.1007/s00134-013-2998-5

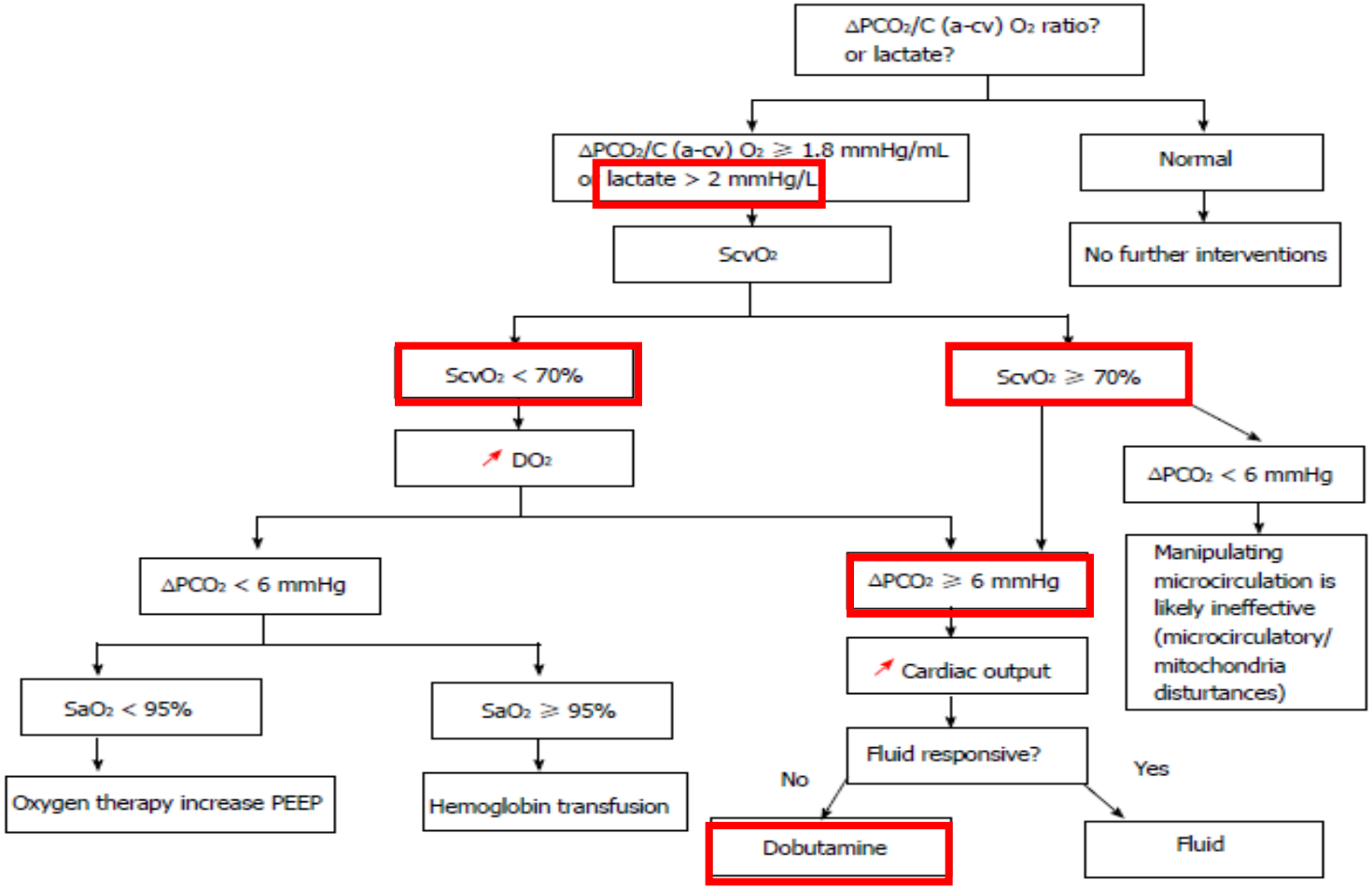
EDITORIAL

B. Vallet
M. R. Pinsky
M. Cecconi

Resuscitation of patients with septic shock: please "mind the gap"!

- 1. Hodnota více než 6 mmHg (0,8 kPa) by mohla přispět k rozhodnutí manipulovat s tekutinami nebo dobutaminem.
- 2. Nejsou velké klinické studie. Rutinně neužíváme. Aktuálně při manipulaci s CO „vystačíme“ s klinikou, (TTE), LiDCO, laktátem a ScvO2.
- 3. Situace, kdy ScvO2 nad 70%, je patologický laktát a delta PCO2 více 6 mmHg…?!

Laktát, ScvO2, delta PvCO2 a resuscitace šoku (a inotropikum)...



Mallat J *et al*. CO_2 gap in septic shock

World J Crit Care Med 2016 February 4; 5(1): 47-56

Závěr – resuscitace šoku v KV

- Cílem je optimalizace tkáňové perfuze.
- Monitorujeme laktát, ScvO2, používáme TTE (typ šoku) a LiDCO.
- Jsme zvědavi na přínos delta PvCO2.
- Prioritou je resuscitace tekutinami (a noradrenalinem).
- Katecholaminy jistě ano, ale s cílem minimálních dávek nejkratší dobu.
- Dobutamin podáváme v pravou chvíli a dle monitorace.
- Levosimendan nepodáváme prakticky vůbec.

Děkuji za pozornost!

Karlovarská
krajská
nemocnice

Ještě méně inotropik a (vasopresorů) v šoku? Cooling!

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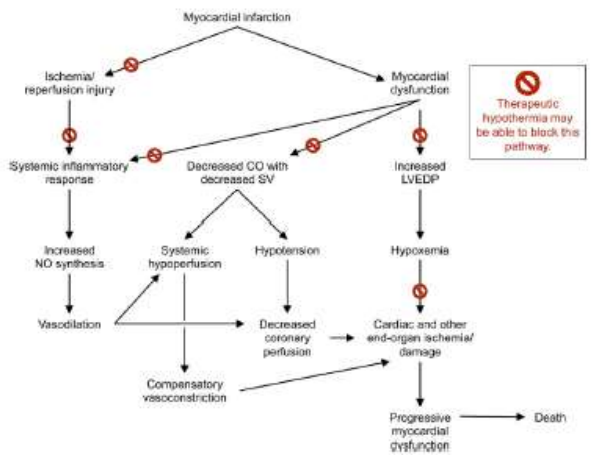
VIEWPOINT

Post-Myocardial Infarction Cardiogenic Shock Is a Systemic Illness in Need of Systemic Treatment

Is Therapeutic Hypothermia One Possibility?

Brian M. Stegman, MD,* L. Kristin Newby, MD, MHS,† Judith S. Hochman, MD,‡
E. Magnus Ohman, MD†

Durham, North Carolina; and New York, New York



Fever Control Using External Cooling in Septic Shock

A Randomized Controlled Trial

Frédérique Schortgen[1,2], Karine Clabault[3], Sandrine Katsahian[4], Jerome Devaquet[5], Alain Mercat[6], Nicolas Deye[7], Jean Dellamonica[8], Lila Bouadma[9], Fabrice Cook[10], Olfa Beji[1], Christian Brun-Buisson[1], François Lemaire[1], and Laurent Brochard[1,2,11]

Rationale: Fever control may improve vascular tone and decrease oxygen consumption, but fever may contribute to combat infection.
Objectives: To determine whether fever control by external cooling diminishes vasopressor requirements in septic shock.
Methods: In a multicenter randomized controlled trial, febrile patients with septic shock requiring vasopressors, mechanical ventilation, and sedation were allocated to external cooling (n = 101) to achieve normothermia (36.5–37°C) for 48 hours or no external cooling (n = 99). Vasopressors were tapered to maintain the same blood pressure target in the two groups. The primary endpoint was the number of patients with a 50% decrease in baseline vasopressor dose after 48 hours.
Measurements and Main Results: Body temperature was significantly lower in the cooling group after 2 hours of treatment (36.8 ± 0.7 vs. 38.4 ± 1.1°C; $P < 0.01$). A 50% vasopressor dose decrease was significantly more common with external cooling from 12 hours of treatment (54 vs. 20%; absolute difference, 34%; 95% confidence interval [95% CI], −46 to −21; $P < 0.001$) but not at 48 hours (72 vs. 61%; absolute difference, 11%; 95% CI, −23 to 2). Shock reversal during the intensive care unit stay was significantly more common with cooling (86 vs. 73%; absolute difference, 13%; 95% CI, 2 to 25; $P = 0.021$). Day-14 mortality was significantly lower in the cooling group (19 vs. 34%; absolute difference, –16%; 95% CI, −28 to −4; $P = 0.013$).
Conclusions: In this study, fever control using external cooling was safe and decreased vasopressor requirements and early mortality in septic shock.

Am J Respir Crit Care Med Vol 185, Iss. 10, pp 1088–1095, May 15, 2012