Journal Meeting

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1. **Diastolic dysfunction and mortality in severe sepsis and septic shock.**
   --- Eur Heart J. 2012 Apr;33(7):895-903
2. **Corticosteroid after etomidate in critically ill patients: A randomized controlled trial.**
   --- Crit Care Med. 2012 Jan;40(1):29-35
3. **Vasopressin for treatment of vasodilatory shock: an ESICM systematic review and meta-analysis.**
   --- Intensive Care Med. 2012 Jan;38(1):9-19
4. **Consensus statement of the ESICM task force on colloid volume therapy in critically ill patients.**
   --- Intensive Care Med. 2012 Mar;38(3):368-83

Diastolic dysfunction and mortality in severe sepsis and septic shock

--- Eur Heart J. 2012 Apr;33(7):895-903

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BACKGROUND

- Sepsis affects ＞600,000 patients/year in the USA, with high mortality: up to 70% in seriously ill patients.
- Cardiovascular system in severe sepsis and septic shock
  - Venous / arterial dilatation → ↓ cardiac preload / afterload
  - Microvascular dysfunction → capillary leak, tissue edema, hypoxia
  - Myocardial dysfunction → haemodynamic derangement
- (1980's) Systolic dysfunction and ventricular dilatation occurred in 50% of septic shock patients despite normal or high cardiac outputs. Paradoxically, patients with systolic dysfunction had better survival and myocardial dysfunction recovered if patients survived the septic course.
- Diastolic dysfunction is currently recognized as a major cause of heart failure despite normal EF and as a serious predictor of long-term mortality and morbidity.

➔ **However, no study had systematically investigated the prognostic role of diastolic dysfunction in septic patients in an adequately sized cohort.**

METHODS

- A cohort of 262 ICU patients with severe sepsis and septic shock underwent two echocardiography examinations, during 2007–2009.
- **Severe sepsis：**
  - ✓ Evidence of infection or serious clinical suspicion for infection
  - ✓ At least two signs of SIRS: (1)temperature ＞38℃ or ＜ 36℃ (2) pulse ＞ 90 b.p.m. (3) respiratory rate ＞20 breaths/min or mechanical ventilation (4) WBC ＞12 000 or ＜4000 or ＞10% bands
  - ✓ At least one organ dysfunction
- **Septic shock：severe sepsis + hypotension**
  - Hypotension = sBP＜90 mmHg；lasting ＞1 h；not responding to fluid therapy (↑ CVP to 12 or 15 mmHg in patients with oliguria)；requiring vasopressor therapy
  - Exclusion criteria :
    - greater than mild mitral and/or aortic valve disease
    - echocardiographic evidence of regional myocardial wall motion abnormality suggesting regional ischaemia or previous infarction
    - poor quality echocardiographic images and measurements

METHODS

- Echocardiography
  - All patients underwent 2 trans-thoracic echocardiography
    - 1st：as early as possible after ICU admission with the diagnosis of sepsis
    - 2nd：on the next day (to confirm stability or differences in results)
- Blood samples
  - Obtained on the 2 days of the echocardiography examinations
    - ✓ high-sensitivity troponin-T (hs-troponin-T) : normal < 0.03 ng/mL
    - ✓ N-terminal pro-B-type natriuretic peptide (NT-proBNP) : normal < 125 pg/mL
- Clinical data
  - All demographic, clinical, haemodynamic, respiratory & lab results, vasopressor therapies, daily fluids administered and balance were prospectively collected.
  - SOFA and APACHE-II scores were calculated on the day of admission with the diagnosis of sepsis.
  - Mortality data were collected from the hospital's registry (minimum period of 6 months and up to 2-year follow-up).

RESULTS

- The study included 262 patients after exclusion.
- The main sources of sepsis were: gastrointestinal,107(41%); multi-trauma with wound infections,39 (15%); respiratory,32 (12%); vascular surgery/limb ischaemia,24(9%); genitourinary,18(7%); orthopaedic/skeletal,19(7%).
- Hypotension occurred in 237 (90.4%) patients.
  In 163 (62%) patients, septic shock persisted despite fluid resuscitation requiring one or more vasoactive medications.
- All patients were tracheally intubated and mechanically ventilated at the time of echocardiography examination due to significant respiratory dysfunction or failure.
- **No** statistically significant differences between the two sequential echocardiography studies in any of the parameters measured. The averaged results were used for further analysis.

RESULTS

Table 1 Clinical and biochemical data of patients who died or survived the hospitalization

	Survived, n = 167 (64%)	Died, n = 95 (36%)	P-value
Age	56 ± 21	70 ± 17	<0.0001
Gender			
Female (%)	63 (38%)	40 (42%)	0.28
Hypertension	51 (30.5%)	47 (49.5%)	0.002
Diabetes mellitus	37 (22.2%)	26 (27.4%)	0.21
Ischaemic heart disease	33 (19.8%)	20 (21.1%)	0.46
Positive blood cultures	59 (35.3%)	48 (50.5%)	0.012
APACHE-II score	18.8 ± 6.5	24.5 ± 7.6	<0.0001
SOFA score	8.7 ± 3.4	10.9 ± 4.3	<0.0001
Heart rate (b.p.m.) mean/max.	92 ± 18/110 ± 18	89 ± 21/109 ± 21	0.21/0.81
Systolic BP (mmHg), mean/min	120 ± 22/87 ± 14	114 ± 28/84 ± 15	0.04/0.018
Diastolic BP (mmHg), mean/min	61 ± 13/48 ± 7	55 ± 19/46 ± 16	0.01/0.19
CVP (mmHg), mean	12.6 ± 5.2	13.7 ± 4.3	0.15
Lowest Hb (g%)	9.7 ± 1.2	9.7 ± 1.2	0.93
Lowest SaO_2 (%)	94 ± 3	92 ± 4	0.001
Lowest pH	7.31 ± 0.08	7.16 ± 0.61	0.002
Creatinine (mmol/L), max.	168 ± 148	250 ± 161	<0.0001
Urine output (mL/24 h/m^2)	1161 ± 624	717 ± 538	<0.0001
Fluid balance (mL/24 h/m^2)	594 ± 800	924 ± 998	0.005
Dialysis	9 (6.1)	12 (14.5)	0.032
Vasoactive medications	95 (56.9)	68 (71.6)	0.012
Cardiac biomarkers			
High-sensitivity troponin-T (ng/mL)	0.04 (0.01–0.11)	0.15 (0.06–0.25)	<0.0001
NT-proBNP (pg/mL)	2275 (567–9426)	13 980 (5877–34 718)	<0.0001

Values are n (%), mean ± SD, and median [inter-quartile range].

RESULTS

Table 2 Echocardiographic data of patients who died or survived the hospitalization

	Survived, n = 167 (64%)	Died, n = 95 (36%)	P-value
LV end-diastolic diameter (cm)	4.6 ± 1.0	4.5 ± 1.1	0.92
LV end-systolic diameter (cm)	2.9 ± 0.8	2.9 ± 0.9	0.20
Isovolumic relaxation time (ms)	49.6 ± 23.4	61.5 ± 54.6	0.017
E wave (cm/s)	95 ± 33	89 ± 22	0.18
A wave (cm/s)	86 ± 52	78 ± 23	0.10
E/A ratio	1.22 ± 0.55	1.22 ± 0.61	0.99
E wave deceleration time (ms)	147 ± 48	144 ± 49	0.67
Velocity of propagation (cm/s)	76.1 ± 42	85 ± 32	0.34
Septal s′ (TDI, cm/s)	10.0 ± 2.9	8.7 ± 3.1	0.003
e′ (TDI, cm/s)	9.3 ± 3.4	6.8 ± 2.2	<0.0001
a′ (TDI, cm/s)	9.9 ± 3.4	8.5 ± 4.0	0.010
Lateral s′ (TDI, cm/s)	11.5 ± 3.7	9.7 ± 3.8	0.001
e′ (TDI, cm/s)	11.3 ± 4.1	9.0 ± 3.5	<0.0001
a′ (TDI, cm/s)	10.1 ± 3.8	8.6 ± 4.4	0.012
LV end-diastolic volume index (cm^3/m^2)	58.6 ± 17.3	51.7 ± 18.4	0.005
LV end-systolic volume index (cm^3/m^2)	23.5 ± 12.7	22.6 ± 15.7	0.63
SV index (cm^3/m^2)	35.1 ± 8.5	29.1 ± 8.7	<0.0001
LVEF (%)	60 ± 10	57 ± 13	0.14
Cardiac index (L/m^2)	3.3 ± 0.9	2.7 ± 0.9	<0.0001
Tricuspid insufficiency gradient (mmHg)	27.4 ± 14.3	31.1 ± 13.4	0.09
RV end-diastolic area (cm^2)	21.2 ± 5.3	20.4 ± 6.7	0.30
RV end-systolic area (cm^2)	13.9 ± 4.4	13.0 ± 4.7	0.13
RV stroke area change (cm^2)	7.4 ± 3.6	7.6 ± 3.8	0.7

Values are mean ± SD.

RESULTS

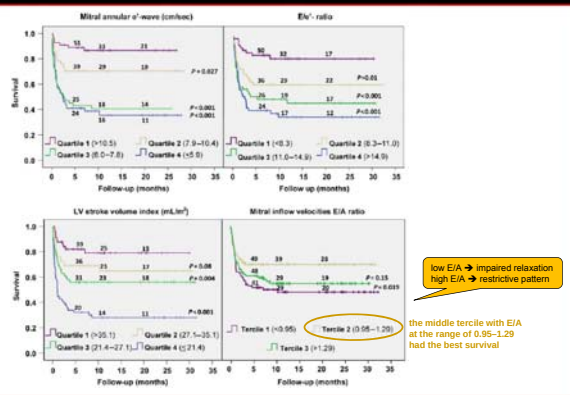
Table 3 The independent predictors of in-hospital and overall mortality

	In-hospital mortality, multivariate logistic regression			Overall mortality, multivariate Cox's regression		
	Odds ratio [95% CI*]	Wald stat.	P-value	Hazard ratio (95% CI*)	Wald stat.	P-value
e′-wave (TDI)	0.70 (0.59–0.84)	15.1	<0.001	0.76 (0.68–0.99)	21.5	<0.001
E/e′ ratio	1.16 (1.07–1.26)*		<0.001	1.08 (1.04–1.13)*		<0.001
APACHE-II score	1.06 (1.01–1.12)	5.7	0.017	1.06 (1.03–1.09)	16.3	<0.001
Urine output (L/24 h/m^2)	0.54 (0.28–0.99)	9.1	0.003	0.65 (0.42–0.99)	9.91	0.002
LVSV index	0.95 (0.91–0.98)	3.9	0.040	0.96 (0.93–0.99)	7.0	0.008
Lowest SaO_2 (%)				0.93 (0.87–0.98)	6.6	0.010
Positive blood culture	2.72 (1.28–5.80)	7.1	0.007			

*CI, confidence interval.

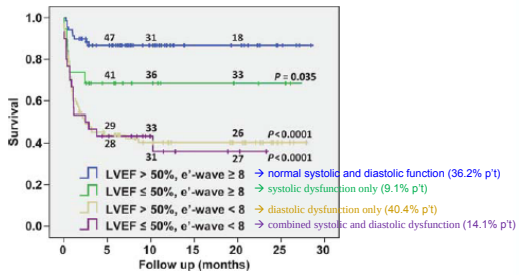
➔ Reduced septal e′-wave (or increased E/e′ ratio) was the strongest independent predictor.

RESULTS



RESULTS

- **Diastolic and systolic myocardial function**



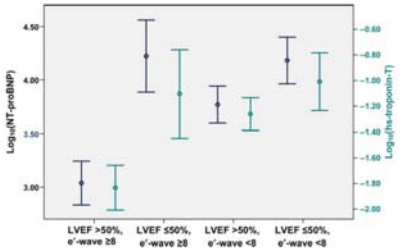
– Patients with LVEF ≤50% only, patients with e′-wave <8 cm/s only, and patients with combined LVEF ≤50% & e′-wave <8 cm/s had worse survival compared with patients having normal systolic and diastolic function.

RESULTS

- **Diastolic dysfunction in relation to age and co-morbidities**
  - Reduced e′-wave velocity correlated strongly with age and less so with hypertension, diabetes mellitus, and history of ischaemic heart disease. [P<0.0001, <0.0001, 0.0008, and <0.0001, respectively]
  - In multivariate survival analyses, only e′-wave and age predicted mortality (e′-wave was the strongest predictor). The other co-morbidities did not gain statistical significance.

RESULTS

- **hs-Troponin-T and NT-proBNP**
  - Both hs-Troponin-T and NT-proBNP were associated with in-hospital and overall mortality.
  - hs-troponin-T was only mildly elevated (median=0.07, IQR:0.02–0.17 ng/mL)
    NT-proBNP reached very high levels(median=5762, IQR:1001–15 962 pg/mL)



DISCUSSION

- **The main findings of this study ：**
  - ◆ Patients with severe sepsis and septic shock frequently suffer from diastolic dysfunction and **diastolic dysfunction is the strongest independent predictor of early mortality**.
  - ◆ Although diastolic dysfunction is associated with age, hypertension, diabetes mellitus, and IHD, diastolic dysfunction is a stronger independent predictor of mortality than age and the other co-morbidities.
  - ◆ Both hs-troponin-T and NT-proBNP are significantly elevated not only in patients with reduced LVEF but also in patients with isolated diastolic dysfunction. Both hs-troponin-T and NT-proBNP predict mortality.

DISCUSSION

- **Diastolic dysfunction and cardiovascular dynamics in sepsis**
  - Fluid loading is one of the mainstays in the haemodynamic management of sepsis to increase cardiac output.
  - Previous studies as well as the present one have shown that excessive fluid loading is associated with greater mortality in septic patients.
    ∵ microvascular dysfunction & increased vascular permeability → interstitial edema with subsequent tissue hypoxia, organ dysfunction, and death
    ∵ non-compliant LV → aggravates lung congestion, leading to pulmonary HTN, RV dysfunction, and further decrease in LV volumes
  - Diastolic dysfunction is strongly associated with age, hypertension, diabetes mellitus, and IHD.
    ➔ diastolic dysfunction was a pre-existing condition in the majority of patients, however, diastolic dysfunction was also significantly aggravated by the acute critical and stressful illness

DISCUSSION

- **Limitations**
  - This is a single-centre study and therefore it is possible that local management strategies of sepsis may have influenced both myocardial function and outcome.
  - Although tissue-Doppler velocity parameters are less load-dependent than flow measurements, they are nevertheless not totally load independent.
  - Inherent difficulty of measuring RV volumes by 2D echocardiography.
  - Since this study did not include follow-up echocardiography examinations, the present data cannot answer whether sepsis was responsible for a transient diastolic dysfunction or whether the observed diastolic dysfunction was a pre-existing condition.

Corticosteroid after etomidate in critically ill patients : A randomized controlled trial

--- Crit Care Med. 2012 Jan;40(1):29-35

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BACKGROUND

- Etomidate is a first-line anesthetic agent used to facilitate endotracheal intubation in hemodynamically unstable patients.
- Single-dose etomidate blocks cortisol synthesis by inhibiting the activity of 11β-hydroxylase that converts 11β-deoxycortisol into cortisol in the adrenal gland, resulting in a primary adrenal insufficiency with effects lasting for up to 48 hrs.

➔ ***To eliminate the use of etomidate ?***
or To add concomitant administration of corticosteroids ?

- Moderate-dose hydrocortisone (200–300 mg/day) has been successfully proposed to overcome critical illness-related adrenal insufficiency, particularly in septic patients responding poorly to fluid resuscitation and vasopressor agents.

➔ ***How about the effectiveness of such supplementation for etomidate-related adrenal insufficiency ?***

METHODS

- **Patient Selection**
  - prospective, randomized, controlled, double-blind (caregiver, investigator)
  - 2008.7~2010.7, the University Hospital of Grenoble (included 3 ICUs)
  - Patients who needed sedation to facilitate endotracheal intubation, through RSI with intravenous single-dose etomidate and suxamethonium.
  - Exclusion criteria :
    - septic shock requiring steroid supplementation
    - chronic adrenal insufficiency
    - pituitary disorder
    - HIV infection
    - concomitant or prior treatment with steroids, ketoconazole, or fluconazole
    - previous corticotrophin stimulation test for reasons other than the study protocol
    - probability of survival ＜ 48 hrs
    - etomidate administration ≧ 24 hrs after patient admission to the ICU
    - Enrollment in the study ≧ 5 hrs after etomidate induction.

METHODS

- **Study Protocol**
  - **H0** (reference time)：the induction time
  - **H6**：completion of clinical data and the blood sampling for the corticotrophin test at H6 (baseline)
  - **H6~H48**：randomly assigned in a 1:1 ratio to HC group (Hydrocortisone, 200 mg/day over a total of 42 hrs infusion) or control group (0.9% NaCl)
  - **H6, H12, H24, H48**：variables were collected respectively, especially the cardiovascular SOFA score
  - Vasopressive support (norepinephrine) was continuously infused to maintain MAP 65~90 mmHg. In severe brain injury, MAP maintained 80~90 mmHg.
  - Insulin was administered to maintain serum glucose ＜10 mmol/L.

METHODS

- **Hormonal Assays**
  - **H5**：high-dose corticotrophin stimulation test (CST) = 250μg synthetic 1-24 adrenocorticotropic hormone
  - **H6, H12, H24, H48**：check serum total cortisol & 11β-deoxycortisol
  - Etomidate-related adrenal insufficiency：
    Δ cortisol＜250 nmol/L (9 μg/dL) after CST,
    associated with 11β-deoxycortisol ＞8 nmol/L (0.28 μg/dL)
- **End Points**
  - **Primary study outcome**：patients with a cardiovascular SOFA score of 3 or 4 at H6, H12, H24, and H48
  - **Secondary study outcomes**：the course of norepinephrine dose, maximum serum glucose, the number of patients treated by insulin, maximum SOFA score, maximum cardiovascular SOFA score, 28-day all-cause mortality, the duration of mechanical ventilation and of ICU stay, the number of ICU days with norepinephrine support

METHODS

SOFA score	0	1	2	3	4
Respirationa PaO_2/FIO_2 (mm Hg) SaO_2/FIO_2	>400	<400 221–301	<300 142–220	<200 67–141	<100 <67
Coagulation Platelets $10^3/mm^3$	>150	<150	<100	<50	<20
Liver Bilirubin (mg/dL)	<1.2	1.2–1.9	2.0–5.9	6.0–11.9	>12.0
Cardiovascular[b] Hypotension	No hypotension	MAP <70	Dopamine </=5 or dobutamine (any)	Dopamine >5 or norepinephrine </=0.1	Dopamine >15 or norepinephrine >0.1
CNS Glasgow Coma Score	15	13–14	10–12	6–9	<6
Renal Creatinine (mg/dL) or urine output (mL/d)	<1.2	1.2–1.9	2.0–3.4	3.5–4.9 or <500	>5.0 or <200

RESULTS

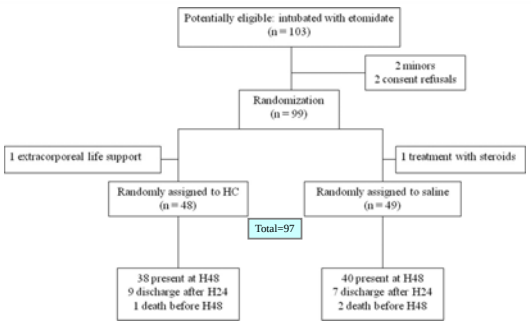

Figure 1. Patient flow diagram showing the number of identified, excluded, and analyzed patients.

HC, hydrocortisone.

RESULTS

Table 1. Characteristics and physiological data collected at the time of etomidate administration (H0) from 97 patients according to their subsequent allocation into treatment groups receiving saline solution (control) vs. hydrocortisone

	Control (n = 49)	Hydrocortisone (n = 48)
Age, yrs	45 (33–59)	52 (34–63)
Male sex, no.	32 (65%)	31 (65%)
Weight, kg	75 (65–80)	70 (65–79)
Patients with body mass index >30, kg/m²	9 (18%)	8 (17%)
Patient history, no.		
Hypertension	10 (20%)	13 (27%)
Coronary artery disease	5 (10%)	6 (13%)
Congestive heart failure	2 (4%)	2 (4%)
Diabetes	6 (12%)	8 (17%)
Reasons for endotracheal intubation, no.		
Isolated severe traumatic brain injury	7 (14%)	11 (23%)
Subarachnoid hemorrhage	5 (10%)	5 (10%)
Multiple trauma	24 (49%)	18 (37%)
Acute poisoning	5 (10%)	7 (15%)
Sepsis with no shock	1 (2%)	2 (4%)
Others	7 (14%)	5 (10%)
Disease severity before intubation, no.		
Glasgow Coma Scale score	12 (7–15)	9 (6–14)
Heart rate, beats/min	89 (74–103)	89 (75–110)
Systolic blood pressure, mm Hg	120 (105–136)	114 (101–130)
Temperature, °C	36.5 (35.7–36.9)	36.5 (35.5–37.0)
Cardiovascular Sequential Organ Failure Assessment	0 (0–1)	0 (0–1)
Etomidate dose, mg/kg	0.33 (0.25–0.46)	0.32 (0.29–0.43)
Simplified Acute Physiology Score II	42 (32–51)	45 (34–54)
Injury Severity Score[a]	27 (21–34)	25 (16–29)

[a]Forty-one missing values; [b]injury Severity Score was not calculated for the 37 nontrauma patients.
Data are median (25th–75th interquartile range) or number (%), unless otherwise specified.

RESULTS

Table 2. Baseline clinical and biological characteristics from 97 study patients collected at H6, before the initiation of treatment, i.e., saline solution (control) vs. hydrocortisone

	Control (n = 49)	Hydrocortisone (n = 48)
Systolic blood pressure, mm Hg	119 (103–131)	120 (101–137)
Diastolic blood pressure, mm Hg	65 (57–72)	61 (56–70)
Mean arterial pressure, mm Hg	85 (73–90)	83 (71–89)
Heart rate, beats/min	75 (65–90)	79 (66–103)
Temperature, °C	36.5 (35.0–37.3)	36.4 (35.4–37.1)
Cardiovascular Sequential Organ Failure Assessment	3 (1–4)	4 (1–4)
Laboratory values		
White blood cells, Giga/L	11.0 (8.6–14.7)	12.1 (9.7–15.3)
Hemoglobin, g/L	114 (103–128)	113 (98–133)
Platelets, Giga/L	178 (125–225)	191 (153–228)
Plasma sodium, mmol/L	141 (139–144)	141 (138–143)
Plasma glucose, mmol/L	7.5 (5.8–9.0)	7.4 (5.9–9.8)
Plasma protein, g/L	50 (44–58)	58 (46–62)
Serum albumin, g/L	28 (24–33)	31 (25–35)
Plasma creatinine, µmol/L	67 (50–89)	71 (52–84)
PaO_2, mm Hg[a]	147 (114–179)	151 (110–198)
$Paco_2$, mm Hg[a]	38 (33–45)	35 (32–40)
Arterial pH[a]	7.36 (7.29–7.40)	7.36 (7.29–7.44)
Arterial lactate, mmol/L	1.8 (1.8–3.1)	1.9 (1.5–3.1)

[a]Eight missing values.
Data are median (25th–75th interquartile range) or number (%), unless otherwise specified.

RESULTS

Table 3. Time course of adrenal function assessment according to treatment, saline solution (control) vs. hydrocortisone[a]

	Before Treatment H5	Before Treatment H6	During Treatment H12	H24	H48
HC/control, no.	(46/47)	(45/46)	(39/45)	(41/43)	(35/35)
Cortisol, nmol/L					
HC	279 (174–457)	425 (289–579)	1383 (1062–2195)[b,c]	1105 (956–1415)[b,c]	1009 (819–1191)[b,c]
Control	317 (187–466)	422 (287–540)	447 (274–651)	368 (196–549)	334 (239–579)
11β-deoxycortisol, nmol/L					
HC	121 (36–190)	165 (112–291)	62 (31–161)[c]	20 (15–61)[c]	10 (8–19)[c]
Control	81 (26–149)	147 (104–275)	115 (58–172)[c]	32 (21–66)[c]	11 (8–34)[c]
Serum albumin, g/L					
HC	30 (24–36)	31 (25–35)	33 (25–36)	32 (26–35)	28 (24–32)[c]
Control	31 (26–33)	28 (24–33)	29 (26–31)	27 (24–32)	26 (22–31)[c]

HC, hydrocortisone.
[a]Treatment was initiated after the completion of a corticotrophin stimulation test (H6). Serum cortisol and 11[β-ketu]-deoxycortisol concentrations (nmol/L) were determined at H5, H6 (baseline), H12, H24, and H48 after single-dose etomidate (H0); [b]$p < .01$ vs. control; [c]$p < .01$ vs. H6. Data are median (25th–75th interquartile range).

RESULTS

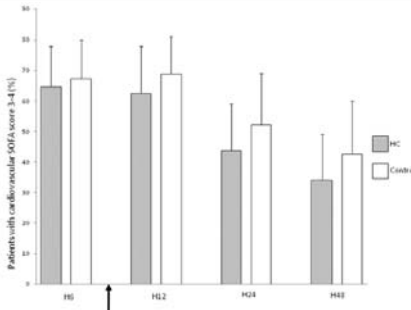

Figure 2. Clinical course of patients with a cardiovascular Sequential Organ Failure Assessment (SOFA) score of 3 or 4, i.e., moderate-to-severe cardiovascular failure at H6 (baseline), H12, H24, and H48 according to their allocated treatment, hydrocortisone (*HC*) vs. saline (control). Treatment was initiated once the data completed at H6 (*arrow*). Data are expressed as median and 95% confidence interval.

RESULTS

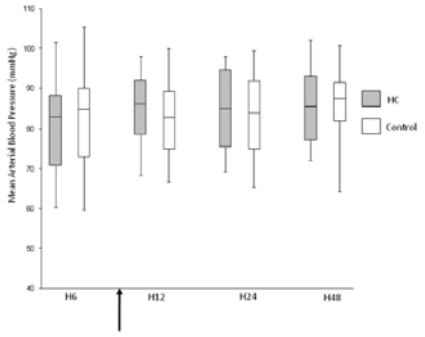

Figure 3. Box (median, 25th and 75th percentiles) and whisker (5th and 95th percentiles) plots of mean arterial blood pressure (in mm Hg) at H6 (baseline), H12, H24, and H48 according to the allocated treatment, hydrocortisone (*HC*) vs. saline (control). Treatment was initiated once the data completed at H6 (*arrow*).

RESULTS

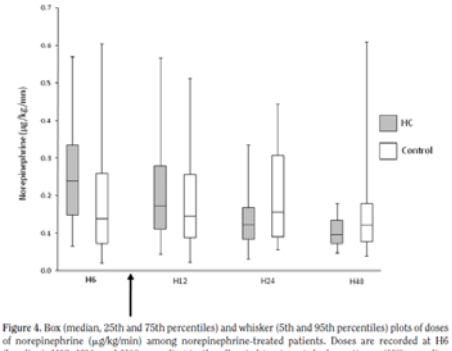

Figure 4. Box (median, 25th and 75th percentiles) and whisker (5th and 95th percentiles) plots of doses of norepinephrine (µg/kg/min) among norepinephrine-treated patients. Doses are recorded at H6 (baseline), H12, H24, and H48 according to the allocated treatment, hydrocortisone (*HC*) vs. saline (control). Treatment was initiated once the data completed at H6 (*arrow*).

RESULTS

Table 4. Secondary patient outcomes according to their treatment, saline solution (control) vs. hydrocortisone

	Control (n = 49)	Hydrocortisone (n = 48)
During the 48-hr study period		
Maximum Sequential Organ Failure Assessment score	7 (5–9)	7 (5–9)
Maximum cardiovascular Sequential Organ Failure Assessment score	4 (2–4)	4 (0–4)
Cumulative fluid loading, mL/kg	39 (25–62)	35 (14–53)
Cumulative blood cell transfusion, no.	0 (0–3)	0 (0–2)
Urine output, mL/hr[a]	94 (75–122)	93 (79–123)
Maximum plasma glucose, mmol/L	8.3 (7.1–9.6)	9.0 (7.8–10.9)[b]
Patients with insulin, no.	15 (31%)	17 (35%)
During the 28-day follow-up		
Intensive care unit duration of stay, days	8 (4–17)	4 (1–10)
Duration of mechanical ventilation, days	4 (1–10)	2 (1–10)
Duration of norepinephrine support, days	2 (1–4)	2 (1–3)
28-day mortality, no.	6 (12%)	6 (13%)

[a]Eighteen missing values; [b]$p < .05$ vs. control.
Data are median (25th–75th interquartile range) or number (%), unless otherwise specified.

DISCUSSION

- Moderate-dose hydrocortisone used to overcome etomidate-related adrenal insufficiency was **not** associated with changes in the proportion of patients with cardiovascular SOFA scores of 3 or 4. Nor did it affect the ICU length of stay, the number of ventilator days, or the 28-day mortality.
  → Etomidate and its resulting transient adrenal derangement play no major role in the evolution of cardiovascular status.

- The treatment was associated with a significant decrease in norepinephrine dose at H24 and H48.
  → Administration of moderate-dose hydrocortisone for < 48 hrs might have enhanced the sensitivity to norepinephrine.

DISCUSSION

- **Limitations**
  - The decision to perform RSI using etomidate was left at the discretion of the in-charge physicians who were then not involved in the subsequent care of the patient once admitted to the ICU.
  - Hydrocortisone supplementation started at H6 to allow time for CST at H5. Whether supplementation given together with etomidate at H0 would affect the present results warrants further investigation.
  - Progressive decline in serum cortisol in the treated group between H12 and H48 was found. A progressive inhibition of the adrenocorticotropic hormone synthesis secondary to hydrocortisone infusion might be also possible.

DISCUSSION

- **Conclusion**
  - Critically ill patients without septic shock did not benefit from hydrocortisone administered to overcome etomidate-related adrenal insufficiency.
  - These findings suggest that single-dose etomidate could be considered in critically ill patients undergoing RSI in the field or in the emergency room without major concerns about its drug-induced hormonal derangement.

Vasopressin for treatment of vasodilatory shock: an ESICM systematic review and meta-analysis

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- **OBJECTIVE:**
  - To examine the benefits and risks of vasopressin or its analog terlipressin for patients with vasodilatory shock.

- **DATA SOURCE:**
  - CENTRAL, MEDLINE, EMBASE, LILACS databases (up to March 2011)
  - Randomized trials of vasopressin or terlipressin v.s. placebo or supportive treatment in adult and pediatric patients with vasodilatory shock.
  - The primary outcome for this review was short-term all-cause mortality.

- **STUDY SELECTION:**
  - 10 randomized trials (1,134 patients). 6 studies were considered for the main analysis on mortality in adults.

- **DATA EXTRACTION AND SYNTHESIS:**
  - The crude short-term mortality was 206 of 512 (40.2%) in vasopressin/terlipressin-treated patients and 198 of 461 (42.9%) in controls [six trials, risk ratio (RR) = 0.91; 95% confidence interval (CI) 0.79-1.05; P = 0.21; I(2) = 0%].
  - There were 49 of 463 (10.6%) patients with serious adverse events in the vasopressin/terlipressin arm and 51 of 431 (11.8%) in the control arm [four trials, RR = 0.90; 95% CI 0.49-1.67; P = 0.75; I(2) = 26%].
  - Meta-regression analysis showed negative correlation between vasopressin dose and norepinephrine dose (P = 0.03).
- **CONCLUSIONS:**
  - Overall, use of vasopressin or terlipressin **did not** produce any survival benefit in the short term in patients with vasodilatory shock. Physicians may value the sparing effects of vasopressin/terlipressin on norepinephrine requirement given its apparent safe profile.

Consensus statement of the ESICM task force on colloid volume therapy in critically ill patients.

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- **PURPOSE:**
  - Colloids are administered to more patients than crystalloids, although recent evidence suggests that colloids may possibly be harmful in some patients.
  - The European Society of Intensive Care Medicine therefore assembled a task force to compile consensus recommendations based on the current best evidence for the safety and efficacy of the currently most frequently used colloids--hydroxyethyl starches (HES), gelatins and human albumin.
- **METHODS:**
  - Meta-analyses, systematic reviews and clinical studies of colloid use were evaluated for the treatment of volume depletion in mixed intensive care unit (ICU), cardiac surgery, head injury, sepsis and organ donor patients.
  - Clinical endpoints：mortality, kidney function and bleeding.
  - Publications from 1960 until May 2011.

- **CONCLUSIONS:**
  - We recommend not to use HES with molecular weight ≥ 200 kDa and/or degree of substitution>0.4 in patients with severe sepsis or risk of acute kidney injury and suggest not to use 6% HES 130/0.4 or gelatin in these populations.
  - We recommend not to use colloids in patients with head injury and not to administer gelatins and HES in organ donors.
  - We suggest not to use hyperoncotic solutions for fluid resuscitation.

Thanks for your listening !