A Systematic Review and International Web-Based Survey of randomized controlled trials in the perioperative and critical care setting: Interventions increasing mortality.

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Argomento: Anestesia generale

Objective: Reducing mortality is a key target in critical care and perioperative medicine. We aimed to identify all nonsurgical interventions (drugs, techniques, strategies) shown by randomized trials, to increase mortality in these clinical settings.

Design: A systematic review of the literature followed by a consensus-based voting process.

Setting: A web-based international consensus conference.

Participants: 251 physicians from 46 countries.

Interventions: We performed a systematic literature search and identified all randomized controlled trials (RCTs) showing significant increase in unadjusted landmark mortality among surgical or critically ill patients. We reviewed such studies during a meeting by a core group of experts. Studies selected after such review advanced to web-based voting by clinicians in relation to agreement, clinical practice, and willingness to include each intervention into international guidelines.

Measurements and Main Results: We selected 12 RCTs dealing with 12 interventions increasing mortality: diaspirin cross linked hemoglobin (92% of agreement among web voters),overfeeding, **nitric oxide synthase inhibitor in septic shock**, human growth hormone, thyroxin in acute kidney injury, intravenous salbutamol in acute respiratory distress syndrome, plasma-derived protein C concentrate, aprotinin in high-risk cardiac surgery, cysteine prodrug, hypothermia in meningitis, methylprednisolone in traumatic brain injury, and albumin in traumatic brain injury (72% of agreement). Overall, a high consistency (ranging from 80% to 90%) between agreement and clinical practice was observed.

Conclusions: We identified 12 clinical interventions with randomized trials showing increased mortality, with non-conflicting, and widely agreed-upon clinicians agreement on a global scale.

	Treatment		Control		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Albumin (Myburgh 2007)	71	214	42	206	1.63 [1.17, 2.26]	
Aprotinin (Fergusson 2008)	47	779	61	1549	1.53 [1.06, 2.22]	
Cysteine prodrug (Morris 2008)	30	101	18	114	1.88 [1.12, 3.16]	
Diaspirin cross linked Hb (Slown 1999)	24	52	8	46	2.65 [1.32, 5.32]	· · · · · ·
Growth hormone (Takala 1999)	61	139	26	141	2.38 [1.60, 3.53]	
HFOV (Ferguson 2013)	129	275	96	273	1.33 [1.09, 1.64]	
Hypothermia (Mourvillier 2013)	25	49	15	49	1.67 [1.01, 2.76]	
Methylprednisolone (Bone 1987)	1052	4985	893	4979	1.18 [1.09, 1.27]	
Methylprednisolone (Roberts 2004)	46	78	17	58	2.01 [1.30, 3.13]	
Metoprolol (Devereaux 2008)	129	4174	97	4177	1.33 [1.03, 1.73]	
NOS inhibitor (Lopez 2004)	259	439	174	358	1.21 [1.06, 1.39]	
Overfeeding (Braunschweig 2015)	16	41	6	38	2.47 [1.08, 5.66]	
Protein C zymogen (Pappalardo 2016)	16	19	8	18	1.89 [1.09, 3.29]	· · · · · · · · · · · · · · · · · · ·
Salbutamol (Gao Smith 2012)	55	161	38	163	1.47 [1.03, 2.08]	
Thyroxine (Acker 2000)	12	28	4	31	3.32 [1.21, 9.12]	│ ———→
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