1. LeoPARDS

Title:	Levosimendan for the Prevention of Acute Organ Dysfunction in Sepsis
Authors:	Tony Gordon et al
Published	NEJM October 2016
Background:	Levosimendan is a novel calcium sensitising inotrope, which could increase contractility without increasing myocardial oxygen demand. also has extra-cardiac effects, including being anti-inflammatory, anti-apoptotic, improving gut perfusion and limiting ischaemia-reperfusion injury.
Hypothesis:	whether levosimendan reduces the severity of organ dysfunction in adults with septic shock
1° Outcome	Mean daily SOFA score in ICU, up to 28 days post randomisation
Design:	multi-centre, placebo-controlled, randomised trial in 34 UK ICUs
When:	2 years: January 2014 to December 2015
Population:	Fluid replete septic shock receiving a vasopressor for at least 4 hours
Intervention:	Levosimendan 0.05 to 0.2 µg/kg/min for 24 hours, without a loading dose
Control:	Matching placebo, which was visually identical
Power Calc:	Allowing for attrition, 516 pts were required to detect a difference of 0.5 points in mean SOFA score with a 90% power at the 5% significance level
Blnding|Allocation	appropriate
Enrolled	516 patients
Baseline	• Similar at baseline. • recruited 16 hours post vasopressor commencement, • mean norad dose of 0.28 µg/kg/min • mean SOFA scores of
Separation	Clearly groups separated, but 13.5% discontinued early, vs 7.7% of placebo for hypotension or tachycardia
1° Outcome	Mean SOFA score: levosimendan 6.68±3.96 vs 6.06±3.89 placebo group (mean difference, 0.61; 95% CI, −0.07 to 1.29; P = 0.053
2° Outcome	• Non significantly increased 28 day mortality 34.5% s 30.9% • Less likely to be weaned from mechanical ventilation over 28 days, HR 0.77 • More SVT

Comments

1.	Levosimendan circulatory SOFA scores were worse
2.	In the subgroup with advanced cardiac monitoring, no apparent difference in cardiac index or stroke volume despite less than 10% of the control group receiving dobutamine
3.	In keeping with the very recently published CHEETAH trial, where levosimendan appeared to have almost no circulatory effects when run at a mean dose of
4.	More patients needed to have levosimendan discontinued than placebo
5.	The levosimendan group required higher doses of noradrenaline to maintain the same mean arterial pressure and also had more tachycardia – expensive, long acting inodilator, without the inotropy
6.	No benefit in any subgroup
7.	Two further trials in the cardiac surgical setting – CHEETAH & LEVO-CT, published last month, both fail to demonstrate any improvements with levosimendan

2. ALPS

Title:	Amiodarone, Lidocaine, or Placebo in Out-of-Hospital Cardiac Arrest
Authors:	Resuscitation Outcomes Consortium Investigators (USA)
Published	NEJM May 2016
Background:	No drug therapy has been shown to improve outcome in cardiac arrest
Hypothesis:	To test whether either antiarhythmic, amiodarone or lidocaine, were beneficial versus placebo in cardiac arrest
Design:	Multi-centre, randomised controlled, tri-group parallel study in the out-of-hospital setting – paramedics from 55 EMS in the USA Supported by Baxter, who supplied the drugs, but had no input otherwise
Population:	Adults with shock-refractory VF or VT after 1 or more defibrillations May 2012 to October 2015: 0f 38,000 patients, 7000 were eligible 4667 were enrolled, with 3026 included in the per-protocol population
Intervention:	Typical body weight: amiodarone 300mg or lidocaine 120mg or placebo, followed by amiodarone 150mg or lidocaine 120mg or placebo no open label antiarrthymics were allowed pre-randomisation
Power Calc:	3000 patients (1000 per arm) were required to provide 90% power to detect a 6.3% increase in rate of survival to hospital discharge (from 29.7% to 23.4%) at either the 2.5% or 5% significance level, depending on which pair were being compared
Blnding|Allocation	Well executed study with excellent followup of 99.5% of patients
Baseline	Groups were well balanced. Study drugs were first administered after a mean of 19 minutes post call to EMS.
1° Outcome	No difference in survival to hospital discharge • amiodarone 24.4% | lidocaine 23.7% | placebo 21.0%
2° Outcome	No difference in survival with favorable neurologic status • amiodarone 18.8% | lidocaine 17.5% | placebo 16.6%

Comments

1.	Study drugs were administered very late to these patients, and quite possibly too late to make a difference - a mean of 19 minutes after the call to the EMS provider
2.	There were a number of mechanistic features suggesting efficacy • Those with a witnessed arrest did better if they received an anti-arrthymic: ◦ for bystander witnessed arrest, survival to hospital discharge was ◦ amiodarone 27.7% | lidocaine 27.8% | placebo 22.7% • Patients in the placebo arm were more likely to require an additional dose of study drug, more shocks or other rhythm-contrl medications • More patients who received lidocaine than placebo had ROSC on hospital
3.	No difference in total adverse events, although more patients in the amiodarone group required pacing: amiodarone 24.4% | lidocaine 23.7% | placebo 21.0%
4.	No differences in important confounders - coronary catheterization, therapeutic hypothermia, and withdrawal of life-sustaining treatments
5.	Trialists say a trial of 9000 would be needed to identify a 3% mortality benefit with amidarone, whcih could translate into 1800 lives saved per year in the USA
6.	Long time to study drugs (19 mins) but injury fromischaemia/reperfusion happens at 10 mins

3. RESCUEicp

Title:	Trial of Decompressive Craniectomy for Traumatic Intracranial Hypertension
Authors:	Peter Hutchinson et al from Addenbrookes
Published	NEJM Sept 2016
Background:	Decompressive craniectomy is used as a therapy for refractory intra-cranial hypertension in the setting of traumatic brain injury, but its effect is uncertain.
Aim:	to assess the effectiveness of secondary craniectomy as a last-tier intervention in patients with TBI and refractory intracranial hypertension Extended Glasgow Outcome Scale
Design:	international, multicenter, parallel-group, superiority, randomized trial Ran for 10 years – 2004 to 2014 52 centres in 20 countries screened 2008 patients. 71% recruited in the UK
Population:	TBI patients aged 10 to 65, with an abnormal scan and an ICP >25 mmHg for 1 to 12 hours despite stage 1 and 2 therapies (have on slide)
Intervention:	• Decompressive craniectomy or further medical management (thio coma) • Either a hemicraniectomy or bifrontal craniectomy
Other Management:	Largely standard management – sedation, analgesia, head elevation, cerebral perfusion pressure > 60 mmHg, mild hypocapnoea, normothermia, normoglycaemia, noronatraemia etc
Power Calc:	400 patients were required to identify a between group treatment effect of 15% (favorable-outcome rate of 45% vs. 60%) with 80% power at the 5% significance level (two-sided), allowing for a loss to follow-up of up to 15%
Blnding|Allocation	Open label, otherwise robust
Baseline	• 408 patients were recruited and 389 evaluated for the primary outcome • Grounds were largely similar at baseline, with the exception of more drugs and alcohol abuse in the surgical group
Separation	The groups separated with regard to ICP
1° Outcome	• The GOS-E distribution differed between the two groups (P<0.001) • At 6 months, decompression resulted in lower rates of mortality but higher rates of higher rates of vegetative state, lower severe disability, and upper severe disability than medical care

Comments

1.	RESCUEicp gives clinicians a foundation for discussing with relatives the likely wishes of patients in the setting of severe traumatic brain injury. We now have some numbers we can base prognoses on.
2.	Unlike the DECRA trial, this study, which was predominantly, over 70%, performed in the UK, investigates decompressive craniectomy in a manner more usual to UK clinicians – i.e. as a final tier rescue therapy for intracranial hypertension.
3.	There are a couple of points to consider • firstly a very high crossover rate. 37% of the medical group received decompression, which would have diluted the effect from decompression • secondly, the trialists reclassified the definitions of favourable and unfavourable outcomes. If a more usual classification was used, decompression would have resulted in similar proportions of favourable outcome as medical therapy

4. VANISH

Title:	Effect of Early Vasopressin vs Norepinephrine on Kidney Failure in Patients With Septic Shock
Authors:	Tony Gordon et al
Published	JAMA August 201
Background:	Based on data from the VASST trial, vasopressin may be more beneficial than noradrenaline in septic shock on renal failure, organ dysfunction & mortality
Design:	factorial (2×2), multicenter, double-blind, randomized clinical trial (vasopressin or noradrenaline) +/- (hydrocortisone or placebo) – then open label hydrocortisone if still hypotensive 18 UK ICUs Feb 2013 to May 2015 6 hour recruitment window
Population:	Adults with septic shock requiring vasopressor
Intervention:	vasopressin (titrated up to 0.06 U/min) or norepinephrine (titrated up to 12 µg/min) with a target MAP of 65-76mmHg. Patients could receive open label catecholamines but these were weaned first. If patients remained hypotensive, hydrocortisone 50mg 6 hourly or placebo taped over 5 days.
Other Management:	Based on surviving sepsis campaign
Power Calc:	400 patients had 80% power to detect a 20 to 25% relative reduction of risk of developing renal failure (AKIN group 3 definition) at 5% significance level assuming baseline incidence of renal failure of 30 to 50%
Blnding|Allocation	Double blind
Baseline	• 412 patient s randomised – approx 105 per group • Groups similar at baseline • Median APACHE II was 24 and 58% of patients required mechanical ventilation at the time of enrollment
1° Outcome	Kidney failure free days – no difference in distribution between V & NA groups no difference in survivors avoiding renal failure (V 57% vs NA 59%) Lower requirement for RRT with vasopressin (25.4% vs 35.3%) no mortality difference (vasopressin 31% vs noradrenaline 27%)

Comments

1.	The study drugs were started at a median of 3.5 hours after the diagnosis of shock
2.	76% were receiving open-label norepinephrine at randomisation, at a median dose 0.16 µg/kg/min
3.	No difference in fluids administered between groups
4.	Less RRT but non significantly higher mortality
5.	Interestingly, no effect seen with hydrocortisone, in contrast with the findings from VASST, & in particular, no interaction between hydrocortisone and vasopressin on outcomes, other than a reduction in vasopressin dose
6.	Confidence interval includes a possible 5 day increase in renal failure free days with vasopressin!

5. REACT 2

Title:	Immediate total-body CT scanning versus conventional imaging and selective CT scanning in patients with severe trauma (REACT-2): a randomised controlled trial
Authors:	Joanne Sierink et al from Amsterdam
Published:	June 2016 Lancet
Background:	Possible mortality benefit from pan-scanning in severe trauma but no high level evidence
Aim:	To compare total-body CT scanning with the standard work-up (conventional radiology supplemented with selective CT scanning) on in-hospital mortality in patients with trauma
Design:	international, multicentre, open-label, randomised controlled trial at four hospitals in the Netherlands and one in Switzerland Ran April 2011 to January 2014
Population:	Adults with • trauma with compromised vital parameters, • clinical suspicion of life-threatening injuries • severe injury (Injury severity score > 16)
Intervention:	Pan scan (head to pubic symphisis), taken in 2 stages (CT of head and neck followed by CT of chest,abdo and pelvis using IV contrast)
Control	Imaging as per ATLS guidelines – chest & pelvic x-rays & FAST scan during primary survey, selective CT scanning as part f secondary survey
Other Management:	Life saving procedues performed during primary survey
Power Calc:	539 patients per group were needed for detection of a difference in mortality of 5% with a power of 80% and a two-sided alpha of 5%
Blnding|Allocation	Computer based allocation
Baseline	5475 patients screened | 1403 randomised 702 to immediate total-body CT scanning | 701 to the standard work-up Groups similar except for slightly more polytrauma pts in pan scan group (67 v 61%)
1° Outcome	No difference in in-hospital mortality 16% vs 16% No difference in subgroups of polytrauma or TBI

Comments

1.	As expected, this was largely a study of young men, in their early 40s
2.	Not overly sick – SBP 130 mmHg | HR 90 | RR 16 | just 7% hypotensive | pH 7.34 & 7.35
3.	There was a small but significant difference in median radiation doses • in the trauma room – panscan 20.9 mSv vs 20.6 mSv • total hospital admission - panscan 21 mSv vs 20.6 mSv
4.	46% of the selective imaging group ended up effectively having a pan-scan
5.	45% of the selective imaging group received less than the minimum total dose of 20 mSv for a panscan
6.	Panscan patients • finished their imaging 7 minutes quicker (30 mins vs 37 mins) • left the ED 9 minutes quicker (63 min vs 72 mins) – non significant

6. ELAIN

Title:	Effect of Early vs Delayed Initiation of Renal Replacement Therapy on Mortality in Critically Ill Patients With Acute Kidney Injury
Authors:	Alexander Zarbock
Published	JAMA May 2016
Background:	Optimal timing of initiation of renal replacement therapy for severe AKI but without life-threatening indications is still unknown
Design:	German single-center randomized clinical trial August 2013 and June 2015
Population:	231 critically ill patients with KDIGO stage 2 (≥2 times baseline or urinary output <0.5 mL/kg/h for ≥12 hours) and plasma neutrophil gelatinase–associated lipocalin level higher than 150 ng/mL
Early Group:	Early (within 8 hours of diagnosis of KDIGO stage 2; (n=112)
Late Group:	Delayed (within 12 hours of stage 3 AKI or no initiation (n=119))
Other Management:	standardised in terms of mode (CVVHDF), anticoagulation (citrate), replacement fluids, and blood flow > 110 ml/min
Power Calc:	230 patients were required to detect an absolute 90 day mortality reduction of 18% (55% to 37%) with 80% power at the 5% significance level
Blnding|Allocation	Open label
Baseline	604 patients were screened and 231 randomised Groups were similar at baseline, including the reasons for the development of AKI
1° Outcome	Early RRT initiation resulted in improved 90 day mortality 55% vs 39% shorter duration of RRT – 9 vs 24 days greater recovery of renal function – 54% vs 39%

Comments

1.	All patients in the early group and 91% of the late group received RRT
2.	Both groups received identical CRRT - venovenous hemodiafiltration – with an effluent flow of 30 ml/kg/hr
3.	The early group received RRT a median of 6 hours post randomisation, whereas the late group received RRT at a median of 25.5 hours
4.	The secondary outcomes were coherent with the primary outcome – based on this trial, it appears early CRRT is beneficial; however, this is a small, single, centre study
5.	Also published at the same time was the French multi-centre AKIKI trial, asking a similar question
6.	Commencing RRT at KDIGO stage 2 renal injury does not reflect contemporary critical care practice and current recommendations would suggest RRT is based on the patient's overall condition
7.	Also published at the same time was the French multi-centre AKIKI trial, asking a similar question

7. AKIKI

Title:	Initiation Strategies for Renal-Replacement Therapy in the Intensive Care Unit Artificial Kidney Initiation in Kidney Injury (AKIKI)
Authors:	Stéphane Gaudry
Published	NEJM May 2016
Background:	Examining whether early or late initiation of RRT is superior
Design:	French multi-centre, open label, RCT; 31 ICUs; September 2013 to January 2016
Population:	Critically ill patients with AKI & requiring either, or both, ventilation & vasoactive support Stage 3 KDIGO AKI no requirement for immediate RRT
Early Group	RRTwas started immediately after randomization
Late Group	RRT was started if at least one of the following criteria was met: • severe hyperkalemia (> 6 mmol/l) • metabolic acidosis (pH <7.15) • pulmonary edema • urea > 40 mmol/l • oliguria for more than 72 hours after randomization
Other Mgt	Mode of RRT was at the discretion of each centre or physician
Power Calc:	546 patients would have 90% power to show a 15-percentage-point lower mortality with the delayed strategy than with the early strategy (55% to 40%) at 60 days at alpha = 0.05
Baseline	5528 patients were screened and 620 were randomised (allowing for loss to follow up & attrition) Groups were similar at baseline - 86% of patients were mechanically ventilated and 85% required vasopressor support. The majority had a diagnosis of sepsis (80%)
1° Outcome	No difference in 60 day mortality – early 41.6% vs late 63.5%

Comments

1.	Fascinating study when compared to ELAIN - Bigger, multi-centre
2.	Delay of just 2 hours from randomisation to RRT in early group and 55 hours in late group
3.	Important differences – just over 50% of the late group received RRT
4.	Big savings in costs and resource use
5.	No difference in clinical outcomes, such as ICU or hospital LOS6.
6.	Earlier recovery of renal function with the late group
7.	Fewer complications with late initiation – less CRBSI & hypophosphataemia
8.	Interesting interaction with regard to timing of RRT – those who never got RRT had best survival (37%), followed by those started early (48%), followed by those started late (62%).
9.	Non-standardised use of RRT is problematic - dose of RRT delivered was not standardised and this may have introduced a confounding variable
10.	Just 30% received CRRT as the sole means of RRT – not reflective of UK practice
11.	One potential advantage of early RRT is the control of fluid balance. Excessive fluid balance has been shown to be detrimental in lung injury and in critically ill patients with renal injury. Although information is provided on diuresis, no data is provided on fluid balance

8. Oxygen ICU

Title:	Effect of Conservative vs Conventional Oxygen Therapy on Mortality Among Patients in an Intensive Care Unit
Authors:	Massimo Girardis et al
Published	JAMA October 2016
Background:	Harm shown from hyperoxia . Direct pulmonary toxicity – interstitial fibrosis & atelectasis. Harm shown in settings of MI, stroke, cardiac arrest. ? "first give O2"
Design:	Italian single-center, open-label, randomized trial March 2010 to October 2012
Population:	Adults with an expected ICU length of stay of 72 hours or longer
Intervention:	FiO_2 to maintain PaO_2 between 9.3-13.3 kPa or arterial oxyhemoglobin saturation (SpO_2) between 94% and 98% (conservative group) (n=216)
Control	FiO_2 at least 0.4 to maintain PaO_2 values up to 20 kPa or SpO_2 values between 97% and 100% (n=218)
Other Management:	This differed for procedures such as intubation, suction and hospital transfer • Control patients received an FiO2 1.0 • Intervention only received supplemental oxygen if SpO2 fell below 94% • Otherwise at discretion of clinician
Power Calc:	660 patients were required to detect a 6% mortality difference (23% to 17%) with 80% power at the 5% significance level. Trial was stopped early after an earthquake damage the recruiting hospital, limiting their ability to enrol patients. An unplanned interim analysis was performed and the statistical advisor and ethics committee both suggested stopping the study
Blnding|Allocation	
Baseline	1045 patients screened, 480 randomised conventional (n = 244) or conservative (n = 236) Convention group patients were slightly sicker
1° Outcome	Conservative)2 target resulted in reduced ICU mortality - 11.6% vs 20.2% Hospital mortality was also lower Mechanical ventilation free hours also favoured the conservative approach (72 vs 48)

Comments

1.	Biologically plausible
2.	Main problem is the early stopping, raising the chance of a type 1 error
3.	Fragility index 3 (in context of 2 patients withdrawing consent and being excluded from the analysis and it being underpowered, this indicates a very fragile study)
4.	Arguably the trial really examined the safety of liberal oxygen administration; in the conventional arm FiO2 was not reduced below 0.4 unless the PaO2 exceeded 20 kPa; and 100% oxygen was given for procedures and transfers. The study reported the frequency of hypoxic events but did not report the corresponding frequency of hyperoxia; of note; the highest recorded patient median time-weighted PaO2 in the conventional group was 29.3kPa
5.	Further trials are required. These may examine true permissive hypoxaemia or at least balance separating oxygenation between groups whilst avoiding excess hyperoxia

9. MACMAN

Title:	Video Laryngoscopy vs Direct Laryngoscopy on Successful First-Pass Orotracheal Intubation Among ICU Patients
Authors:	Jean Baptiste Lascarrou from Nantes for the the Clinical Research in Intensive Care and Sepsis (CRICS) Group
Published	JAMA January 2017
Background:	There is increasing use of video laryngoscopes but it is unknown if this imporves intubation success rates in the ICU
Design:	• French multi-centre (7 ICUs) RCT – May 2015 to January 2016. Open label, institution-sponsored. Stratified by centre and expertise (expert or non expert). • "Experts" – 5 years of ICU experience OR 1 year of ICU and 2 years of anaesthesia experience | "Non-expert" – All others • Both forms of intubation considered standard of care so specific consent not required.
Population:	Adult ICU patients requiring orotracheal intubation for mechanical ventilation
Intervention:	McGrath laryngoscope vs MacIntosh laryngoscope
Other Management:	All patients received a general anaesthetic. Pre-ox with 100% oxygen either with (1) bag/valve/mask or (2) non-rebreather mask or (3) NIV or (4) HFNO. Hyponotic & relaxant – typically etomidate & sux or ketamine | rocuronium
Power Calc:	Expected 1st pass success rate 65%. To detect an increase to 80% with the McGrath, with a power of 90% at the 5% significance level, 340 patients were needed.
Blnding|Allocation	Open label
Baseline	371 recruited. Groups equal at baseline. 84% of 1st attempts was by non-experts.
1° Outcome	No difference in primary outcome of 1st pass success – McGrath 67.7% vs MacIntosh 70.3%

Comments

1.	High recruitment rate – 371 out of 489
2.	Appeared to be non-anaesthetistic intubators - ? relevance for UK
3.	Didn't use a stylet for first attempt, as per French guidelines. Could use a bougie, which was used more in the McGrath group.
4.	Failures in the McGrath group were due to an inability to pass the tube, in rhe MacIntosh group, due to lack of visualisation of the glottis.
5.	Higher 1st pass success rates for experts than non-experts – 92% vs 65%
6.	More life-threatening complications in McGrath group (9.5 vs 2.8)
7.	The glottic view was significantly improved with the McGrath (pprox 80%), however the intubation success was the same. There may have been an issue with technique or training or perhaps just reflects what a number of people report anecdotally – view easier but does not necessarily to equate to an easier intubation
8.	This trial is really a comparison of the McGrath and the Macintosh, and not a global view of VL versus DL
9.	Interestingly the glottis was only seen in 29% of the DL group. Seems very low, esp as the Cormack-Lehane grade was 1 or 2 in just over 80%
10.	Non patient centred primary outcome – although no difference in patient centred 2 outcomes

10. Hernandez HFNO Trials

Title:	Effect of Postextubation High-Flow Nasal Cannula vs face mask oxygen in low risk patients
Authors:	Gonzalo Hernandez et al from Madrid
Published	JAMA March 2016
Background:	Studies to date have included patients at both low riak and high risk for extubation failure – this study aimed to specifically test HFNO in patients at low risk for extubation failre
Design:	Both parallel group, RCTs FM trial – 7 Spanish ICUs
Population:	Patients receiving MV for at least 12 hours in ICU & at low risk for re-intubation post extubation – multiple criteria defining low risk Age <65; APACHE II score on day of extubation <12; BMI <30; adequate secretions management; simple weaning; <2 co-morbidities; mechanical ventilation <7 days; absence of: heart failure, moderate-to-severe chronic obstructive pulmonary disease, airway patency problems. Patients who were hypercapnic during the spontaneous breathing trials were also excluded
Intervention:	HFNO – started at 10 l/m and increased until discomfort; $Fi0_2$ modified to maintain SpO_2 > 92% and continued for 24 hours Conventional oxygen therapy was applied continuously through nasal cannula or nonrebreather facemask, and oxygen flow was adjusted to maintain SpO_2 greater than 92%
Other Management:	Low risk FM Trial: - 527 patients (264 HFNO & 263 conventional oxygen therapy) Clearly defined criteria for readiness to wean and also reintubation
Power Calc:	Low Risk FM Trial – 520 pts required to identify a 5% absolute risk reduction in extubation failure from 13% to 8% with 80% power and a 2-sided alpha of 5%
Blnding|Allocation	Open label
Baseline	1739 screened & 527 randomised - 264 HFNO & 263 O_2 Groups similar at baseline, but HFNO group ventilated for median 1 day vs FM 2 days
1° Outcome	Low risk FM Trial: Reintubation within 72 hours was lower in HFNO 4.9% vs 12.2% difference was mainly attributable to a lower incidence of respiratory-related reintubation in the high-flow group: 1.5% vs 8.7%

Comments

1.	Timely trial as HFNO appears to be used more and more
2.	Systematic definitions for (1) low risk patients (2) readiness to wean (3) extubation failure
3.	Less post-extubation respiratory failure in HFNO group 8.3 vs 14.4
4.	No difference in median time to reintubation (HFNO 19 hours vs FM 15 hours) – safety concern as delay to reintubation is associated with harm
5.	Is a 12% reintubation rate high for a low risk group?
6.	HFNO works in a number of ways – warms & humidifies inspiratory gases, prevents hypoxia, decreases work of breathing, contributes a small amount of PEEP, improves secretion clearance
7.	Fragility Index was only 5. 4.7 patients in the conventional group that required re-intubation for laryngeal oedema

11. Hernandez HFNO Trials

Title:	Effect of Postextubation High-Flow Nasal Cannula vs Noninvasive Ventilation on Reintubation and Postextubation Respiratory Failure in High-Risk Patients
Authors:	Gonzalo Hernandez et al from Madrid
Published	JAMA October 2016
Background:	To test if HFNO is noninferior to NIV for preventing postextubation respiratory failure and reintubation in patients at high risk of reintubation
Design:	• Both parallel group, non-inferiority, RCTs in • 3 Spanish ICUs • September 2012 to October 2014
Population:	• critically ill adult patients receiving MV > 12 hours • ready for planned extubation • with at least 1 high-risk factors for reintubation Age >65; APACHE II score on day of extubation >12; BMI >30; were ventilated due to heart failure, suffered from mod-severe COPD, had more than 2 pre-defined co-morbidities, were unable to adequately maange respiratory secretions, were at risk of laryngeal oedeam, had previously failed a trial of extubation or had prolonged MV (>7 days)
Intervention:	HFNO – started at 10 l/m and increased until discomfort; $Fi0_2$ modifeid to maintain SpO_2 > 92% and continued for 24 hours NIV delivered continuously for 24 hours, with PEEP/PS modified for a RR 25/min and adequate gas exchange (SpO_2 > 92%). Oxygen flow was also adjusted to maintain SpO_2 greater than 92%
Other Management:	No sedation allowed
Power Calc:	Baseline reintubation rate estimated to be 20 – 25%. With a non-inferiority margin of 10%, and an alpha of 5% and a beta of 80%, 300 patients per group were required, allowing for 15% patient loss.
Blnding|Allocation	Open label
Baseline	5187 screened & 604 randomised - 290 HFNO & 314 NIV Groups largely similar at baseline, although more surgical patients in HFNO group At 12 hours post extubation, the NIV group received
1° Outcome	No difference in primary outcome of reintubation rate at 72 hours – HFNO 22.8% vs NIV 19.1%.

Comments

1.	No difference in respiratory related reintubations – HFNO16.9% vs NIV 15.9%
2.	More respiratory failure in the NIV group – 39.8% vs 26.9%
3.	No difference in median time to reintubation – HFNO 26.5 hours vs NIV 21.5 hours
4.	Total NIV time was 14 hours – very short (although FLORALI may have been shorter still !)
5.	Switch to conventional oxygen therapy at 24 hours - ? not reflective of usual practice – pt gets what they need
6.	NIV group were more hypoxaemic and need a higher FiO2 (40% vs 35%)

END