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Lass Klitgaard, Thomas; Schjørring, Olav Lilleholt; Lange, Theis; Møller, Morten Hylander; Perner, Anders; Rasmussen, Bodil Steen; Granholm, Anders

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Conclusion. Although lower MPP and longer duration of MPP < 60 mmHg were associated with AKI progression, greater MPP-deficit or longer duration of MPP-deficit > 20% was not associated with AKI progression.

Reference(s)

- KDIGO. KDIGO clinical practice guideline for acute kidney injury. Kidney Int Suppl. 2012;2:1–138.
- Saito S, Uchino S, Takinami M, et al. Postoperative blood pressure deficit and acute kidney injury progression in vasopressor-dependent cardiovascular surgery patients. Critical care (London, England). 2016;20:74.

000234

Bayesian and heterogeneity of treatment effect analyses of the HOT-ICU trial

T. Klitgaard¹; OL. Schjørring¹; T. Lange,²; M. Hylander Møller³; A. Perner³; BS. Rasmussen,¹; A. Granholm³

¹Department of anesthesia and intensive care medicine, Aalborg University Hospital, Aalborg, Denmark; ²Department of public health, section of biostatistics, Copenhagen University, Copenhagen, Denmark; ³Department of intensive care, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark

Correspondence: T. Klitgaard

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Introduction. Oxygen is the most commonly administrated medicine in the intensive care unit (ICU). However, its harms and benefits are still not fully elucidated. In the Handling Oxygenation Targets in the Intensive Care Unit (HOT-ICU) trial[1], 2928 adult ICU patients with acute hypoxaemic respiratory failure were randomised to a lower oxygenation target (arterial oxygen tension (PaO $_2$): 8 kPa) or a higher oxygenation target (PaO $_2$: 12 kPa) throughout their ICU admission for up to 90 days. The relative risk (RR) for the primary outcome (90-day all-cause mortality) in the primary, frequentist analysis was 1.02 (95% confidence interval: 0.94–1.11, p=0.64). By using Bayesian analyses we assessed the probabilities of harmful and beneficial effects of a lower oxygenation target and the extent of such effects. Additionally, we explored whether heterogeneity of treatment effects (HTE) was present based on several baseline parameters.

Objectives. In the HOT-ICU intention-to-treat cohort we re-evaluated the effects of a lower versus a higher oxygenation target on mortality, assessed the probability of a range of effect sizes for mortality, and evaluated HTE regarding mortality according to the following baseline variables: Sequential Organ Failure Assessment (SOFA) score, PaO₂/fraction of inspired oxygen (FiO₂) ratio, noradrenaline dose, and plasma lactate concentration.

Methods. Prespecified[2] secondary Bayesian analysis of the primary outcome with assessment of HTE for prespecified baseline variables using adjusted Bayesian logistic regression models with weakly informative priors; models for assessing HTE included the baseline variable of interest and an interaction between this variable and the intervention (lower oxygenation target). Results are presented as posterior probability distributions, summarised with median values and 95% credibility intervals (Crl). RRs < 1 indicate benefit from the lower oxygenation target; RRs > 1 indicate benefit of the higher oxygenation target. HTE is presented using conditional effect plots and as probabilities of negative/positive interactions between baseline variables and the intervention (relatively lower/higher risk of 90-day mortality, respectively, with the lower oxygenation target for increasing values of the baseline variable of interest).

Results. In total, 2888 of 2928 patients (98.6%) were included; adjusted RR = 1.02 (95% Crl: 0.93–1.11). Probabilities of an RR < 0.80, < 0.90, < 1.00, > 1.00, > 1.11 and > 1.25 were 0.0%, 0.3%, 36.5%, 63.5%, 2.0% and 0.0%, respectively. In the HTE analysis (Fig. 1) the probabilities of negative/positive interactions were 35/65% for increasing baseline SOFA scores; 14/86% for increasing baseline lactate concentrations, 76/24% for increasing baseline PaO₂/FiO₂-ratios; and 5/95% for increasing baseline noradrenaline doses.

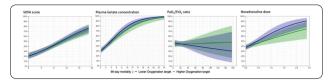


Fig. 1.Conditional effect plots illustrating the potential interaction between treatment allocation and 90-day all-cause mortality on the continuous scale. The values of the individual parameters of interest were plotted on the X-axes; the probabilities of mortality were plotted on the Y-axes.

Conclusion. In this secondary Bayesian analysis of the HOT-ICU trial, the adjusted RR for 90-day all-cause mortality, when comparing a lower and a higher oxygenation target, was with 95% probability between 0.93 and 1.11. Large effect sizes were unlikely. Our results suggested heterogeneity of treatment effects between baseline noradrenaline dose and oxygenation target allocation.

Reference(s)

- Schjørring OL, Klitgaard TL, Perner A, Wetterslev J, Lange T, Siegemund M, Bäcklund M, Keus F, Laake JH, Morgan M, Thormar KM, Rosborg SA, Bisgaard J, Erntgaard AES, Lynnerup A-SH, Pedersen RL, Crescioli E, Gielstrup TC, Behzadi MT, Poulsen LM, Estrup S, Laigaard JP, Andersen C, Mortensen CB, Brand BA, White J, Jarnvig I-L, Møller MH, Quist L, Bestle MH, Schønemann-Lund M, Kamper MK, Hindborg M, Hollinger A, Gebhard CE, Zellweger N, Meyhoff CS, Hjort M, Bech LK, Grøfte T, Bundgaard H, Østergaard LHM, Thyø MA, Hildebrandt T, Uslu B, Sølling CG, Møller-Nielsen N, Brøchner AC, Borup M, Okkonen M, Dieperink W, Pedersen UG, Andreasen AS, Buus L, Aslam TN, Winding RR, Schefold JC, Thorup SB, Iversen SA, Engstrøm J, Kjær M-BN, Rasmussen BS. Lower or Higher Oxygenation Targets for Acute Hypoxemic Respiratory Failure.N Engl J Med 2021; 384: 1301–11.
- The Handling Oxygenation Targets in the Intensive Care Unit (HOT-ICU) trial is funded by Innovation Fund Denmark (4108-00011A), the Novo Nordisk Foundation, the Obel Family Foundation, the Danish Regions' Medicine Foundation, the Danish Society of Anaesthesiology and Intensive Care Medicine, and the Danish Intensive Care Symposium Hindsgavl.
- Klitgaard TL, Schjørring OL, Lange T, Møller MH, Perner A, Rasmussen BS, Granholm A. Bayesian and heterogeneity of treatment effect analyses of the HOT-ICU trial—a secondary analysis protocol. Acta Anaesthesiol Scand 2020; 1–6

000235

Correlation between nutrition, phosphate level and length of ventilation

L. Statlender¹; M. Hellerman¹; G. Fishman¹; I. Kagan¹; I. Bendavid¹; M. Makalde¹; R. Orit²; P. Singer¹

¹Intensive Care Unit, Rabin Medical Center, Petakh Tikwa, Israel; ²Industrial engineering and management, Ariel University, Ariel, Israel

Correspondence: L. Statlender

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Introduction. Hypophosphatemia has been related to prolonged ventilation and may be correlated with increased mortality. Starting or restarting nutrition to the critical care patient is associated with refeeding and hypophosphatemia. The aim of our study is to elucidate the relation between nutrition, hypophosphatemia and length of ventilation.

Methods. A retrospective cohort study included 1374 admissions in two consecutive years. Using the medical electronic chart, demographic and clinical data were obtained, including total administrated calories during admission. We correlated each patient minimal phosphate level with admission outcomes. ROC curve suggested a threshold level for defining hypophosphatemia. Based on this threshold, comparisons between baseline characteristics and outcomes of hypophosphatemic and non-hypophosphatemic patients were performed. Correlation between caloric intake,