2022 CAS Annual Meeting

Cardiovascular and Thoracic

(Abstracts and Case Report/Series)

Contents

Bleeding in Patients with End-Stage Liver Disease Undergoing Liver Transplantation and Fibrinogen Level: A Cohort Study

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Introduction:

Liver transplantation is a surgery with significant bleeding often requiring red blood cell transfusion.[1,2] Many determinants of bleeding and transfusion have been reported in this population. Among them, fibrinogen level is reported as an important one.[3] Arbitrary fibrinogen transfusion thresholds ranging from 1.0 to 2.0 g/L have been suggested in many populations, but no high-quality data supports this recommendation in liver transplant recipients.[3,4] Few studies explored the association between preoperative fibrinogen level and bleeding-related outcomes in patients with end-stage liver disease undergoing liver transplantation. In addition, none has robustly evaluated the threshold at which such association is clinically significant in this population.[5] Our objective was to assess the association between the preoperative fibrinogen level and multiple outcomes related to perioperative blood loss.

Methods:

We conducted a cohort study at one Canadian centre. We included all consecutive patients with end-stage liver disease undergoing liver transplantation. Our primary outcome was intraoperative blood loss. Our secondary outcomes were estimated perioperative blood loss (intraoperative and up to 48 hours after surgery), any intraoperative red blood cell transfusion, any perioperative red blood cell transfusion (intraoperative and up to 48 hours after surgery), any bleeding-related intervention and one-year graft and patient survival. No patient received any blood product containing fibrinogen from the preoperative fibrinogen level measurement to the start of surgery. We estimated linear regression models and marginal risk models adjusted for the following confounders (selected based on their potential causal association with both the fibrinogen level and our outcomes): age, sex, MELD, presence of a hepatocellular carcinoma, preoperative hemoglobin level, INR, PTT, platelet count, creatinine level, preoperative renal replacement therapy, baseline central venous pressure and

the intraoperative use of a phlebotomy. We reported dose-response curves, mean differences and marginal risk differences with 95% confidence intervals.

Results:

We included 613 patients. In both unadjusted and adjusted models, a lower fibrinogen level was associated with higher intraoperative blood loss, higher estimated perioperative blood loss and a higher risk of intraoperative and perioperative red blood cell transfusions (non-linear effects, see figures), but had no effect on other outcomes. We observed a linear increased risk of bleeding and transfusion when the preoperative fibrinogen level was below a value between 2.5 and 3.0 g/L. Based on dose-response curves, a preoperative fibrinogen level of 1 g/L was associated with a higher mean intraoperative blood loss of 0.26 L [0.08 L, 0.45 L], a higher mean estimated perioperative blood loss of 0.58 L [0.18 L, 1.01 L], a higher risk of intraoperative red blood cell transfusion of 22.5% [13.2%, 31.6%] and a higher risk of perioperative red blood cell transfusion of 35.7% [25.8%, 44.8%], compared to a preoperative fibrinogen level of 3.0 g/L.

Discussion:

For patients undergoing liver transplantation for end-stage liver disease, we observed that a preoperative fibrinogen level below a value between 2.5 and 3.0 g/L had a robust and linear association with higher blood loss and higher risk of red blood cell transfusion. These results suggest that such fibrinogen level may not be sufficient for effective hemostasis during surgery. Our findings may improve the selection of high-risk patients with end-stage liver disease undergoing liver transplantation who may require the administration of preoperative fibrinogen to reduce blood loss or red blood cell transfusion. This preemptive intervention should be further studied.

References:

1. Massicotte L, Carrier FM, Denault AY, Karakiewicz P, Hevesi Z, McCormack M, Thibeault L, Nozza A, Tian Z, Dagenais M, Roy A: Development of a Predictive Model for Blood Transfusions and Bleeding During Liver Transplantation: An Observational Cohort Study. J Cardiothorac Vasc Anesth 2018; 32:1722–30
2. Massicotte L, Sassine M-P, Lenis S, Seal RF, Roy A: Survival rate changes with transfusion of blood products during liver transplantation. Can J Anesth Can Anesth 2005; 52:148–55
3. Kozek-Langenecker SA, Ahmed AB, Afshari A, Albaladejo P, Aldecoa C, Barauskas G, De Robertis E, Faraoni D, Filipescu DC, Fries D, Haas T, Jacob M, Lancé MD, Pitarch JVL, Mallett S, Meier J, Molnar ZL, Rahe-Meyer N, Samama CM, Stensballe J, Van der Linden PJF, Wikkelsø AJ, Wouters P, Wyffels P, Zacharowski K: Management of severe perioperative bleeding. Eur J Anaesthesiol 2017; 34:332–95
4. Levy JH, Goodnough LT: How I use fibrinogen replacement therapy in acquired bleeding. Blood 2015; 125:1387–93
5. Bezinover D, Dirkmann D, Findlay J, Guta C, Hartmann M, Nicolau-Raducu R, Mukhtar AM, Moguilevitch M, Pivalizza E, Rosenfeld D, Saner F, Wray C, Wagener G, West J: Perioperative Coagulation Management in Liver Transplant Recipients. Transplantation 2018; 102:578–92

Figure 1:

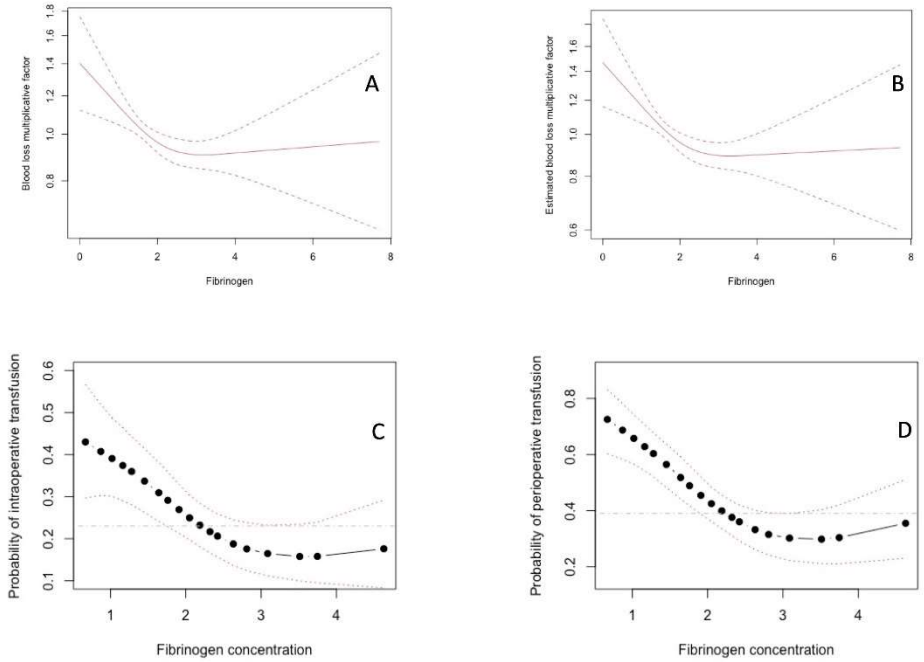

Figure. Effects of fibrinogen level on blood loss and transfusion risk from models adjusted for potential confounders.
A: Intraoperative blood loss. B: Perioperative estimated blood loss. C: Intraoperative transfusion risk. D: Perioperative transfusion risk.

Endovascular Vena Cavae Occlusion in Right Anterior Mini-Thoracoscopic Approach for Tricuspid Valve in Patients with Previous Cardiac Surgery

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Introduction:

Isolated tricuspid valve (TV) surgery is a highly complex intervention usually performed in a population of patients with multiple comorbidities. Recent studies suggest an early mortality rate ranging from 3.9% to 46.9% (1). Redo TV operations represent an even higher surgical challenge due to the presence of adhesions resulting in a more difficult to approach anatomical site. Endovascular vena cavae occlusion (EVCO) is an innovative technique aimed at enhancing exposure to the surgical field. The purpose of this work was to evaluate the clinical feasibility and safety of an EVCO approach in right anterior mini-thoracoscopic TV surgery in patients with previous cardiac surgery.

Methods:

We conducted a retrospective single-center review of patients who underwent a TV repair or replacement by a right anterior mini-thoracoscopic approach with EVCO between 2008 and 2021. Thirty-one patients were included. No exclusion criteria were applied. TV operations were either isolated or concurrently performed with a mitral valve surgery or Maze procedure. The main outcomes measured included the success rate of the bicaval occlusion technique and the mortality rate. Secondary outcomes consisted of post-operative complications (e.g. AKI), reinterventions, and transesophageal echocardiography findings.

Results:

Mean age was 64.9 ± 13.6 years. Thirty patients (96.8%) had moderate to severe tricuspid regurgitation (TR). The mean pre-operative EuroSCORE II was 11.6 ± 9.8. Isolated tricuspid repair or replacement was performed in 14 patients (45.2%), while mitral valve repair or replacement was concurrently done in the remaining 17 patients (54.8%). Endovascular bicaval occlusion was successful in all patients with no reported perioperative complication. Mean cardiopulmonary bypass time was 116.3 ± 45.8 min. Eight patients (25.8%) required surgical reintervention, either for hemostasis (n=5, 16.1%) or for hemodynamic instability (n=3, 9.7%). AKI was present in eight patients (25.8%) in the immediate postoperative period. Median maximum perioperative lactate was 2.7 mmol/L. Median length of stay in the ICU was 6 days. At discharge, 3 patients (10.7%) had moderate TR and none had severe TR. In-hospital mortality rate was 12.9 % (n=4).

Discussion:

This study demonstrates that EVCO is an innovative technique to allow maximal surgical site exposure with minimal dissection in right mini-thoracoscopic TV reoperation. This study reveals the perioperative safety and effectiveness of this technique. The precarious health status of the patients requiring this surgery as well as the inherent morbidity associated with this surgical intervention explains, as predicted by a cardiac operative risk evaluation score (EuroSCORE II), the high mortality rates reported.

References:

1. Sarris-Michopoulos P, Macias AE, Sarris-Michopoulos C, et al. Isolated tricuspid valve surgery - Repair versus replacement: A meta-analysis. J Card Surg. 2022; 37:329-335. doi:10.1111/jocs.16131

Mesenchymal Stem Cell Extracellular Vesicles as a Novel, Regenerative Nanotherapeutic for Myocardial Infarction: A Preclinical Systematic Review

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Introduction:
Despite advances in medical and interventional treatments, perioperative myocardial infarction (MI) remains associated with significant morbidity and mortality. Preclinical studies have suggested that mesenchymal stromal cells (MSC) improve left ventricular function and reduce infarct size following MI. However, manufacturing, storage, and administration of MSCs remain challenging, which precludes widespread clinical adoption. Extracellular vesicles are nanosized particles secreted by MSCs that have been shown to carry biologically active cargo, enabling them to modulate inflammatory and regenerative responses. Hence, MSC-derived extracellular vesicles (MSC-EVs) may offer a novel, safer cell-free alternative to live cell therapy. This systematic review identified and summarized preclinical studies investigating the therapeutic efficacy of MSC-EVs in the context of MI to inform future clinical translation.

Methods:
Ethics review was not required for this study. A systematic search of Ovid MEDLINE®, Embase, and BIOSIS was conducted. All preclinical, controlled interventional studies that compared MSC-EV therapy to placebo using in vivo models of MI were included. Citation screening and data extraction were performed independently by two reviewers. The primary outcome was left ventricular ejection fraction (LVEF); secondary outcomes included LV fractional shortening (LVFS) and infarct size. Random effects inverse variance meta-analysis was conducted. Subgroup analyses identified EV characteristics or methods associated with improved efficacy. Outcomes were pooled using mean difference analysis and presented with 95% confidence intervals (CI). $P<0.05$ was considered statistically significant. Protocol registration: PROSPERO CRD 42019158003.

Results:
Our search strategy identified 1038 records with 58 studies meeting eligibility criteria. All studies utilized mouse (39%) or rat (61%) models of MI with EVs injected acutely following disease induction. Pooled analysis demonstrated preserved cardiac function in animals treated with MSC-EVs. Specifically, MSC-EVs restored LVEF to normal levels (51.7%, CI 49.4–54.0) as compared to placebo (35.0%, CI 32.7–37.3) (Figure 1). Furthermore, LVFS was improved by 9.3% (CI 8.1–10.5) (MSC-EV group 26.1%, CI 24.6–27.5, and placebo group 16.3%, CI 15.2–17.4) (Figure 1). Analysis of cardiac histopathology indicated a 12.2% (CI 10.3–14.0) reduction to infarct size from MSC-EV delivery (Figure 1). From subgroup analyses of LVEF, MSC-EVs showed equivalent efficacy for both sexes and animal species. Tissue source of MSCs including bone marrow, adipose or umbilical cord were

equally protective. Interestingly, the therapeutic efficacy in genetically modified MSC-EVs (e.g. overexpression of target proteins/RNAs) was enhanced considerably as compared to unmodified EVs ($P<0.001$).

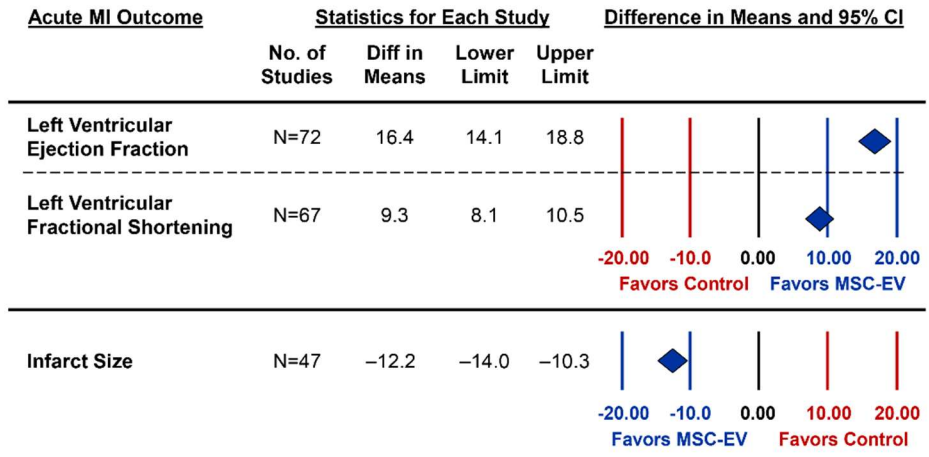
Discussion:

This study is one of the first systematic reviews to investigate the potential therapeutic effects of MSC-EV therapy in preclinical animal models of MI. Our results suggest that treatment with MSC-EVs can markedly attenuate infarct size and drastically improves cardiac function to near normal levels. The opportunity to manipulate the expression of bioactive cargo within EVs creates an intriguing new domain of regenerative medicine to further optimize this novel nanotherapeutic. This review will hopefully help guide future preclinical study design and provides evidence for the potential translational application of MSC-EVs in patients with perioperative MI.

References:

No References.

Figure 1:



Nephrectomy Negatively Impacts Physiological Mechanisms That Maintain Rat Brain Oxygenation Following Acute Hemodilutional Anemia

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Introduction:

Anemia is associated with acute kidney injury (AKI) and stroke in perioperative patients **[1-3]** demonstrating potential vulnerability of these two organs during anemia. Evidence supports that the kidney may be a critical sensor of changes in blood oxygen content (CaO_2) and this function may initiate cardiovascular responses, including increased cardiac output and cerebral blood flow, which preserve brain oxygenation during anemia. We performed acute nephrectomy to test the hypothesis that the kidney is essential in maintaining brain tissue oxygen tension during acute hemodilutional anemia.

Methods:

With Animal Care and Use Committee approval, in accordance with ARRIVE-2 guidelines, we performed sham or bilateral nephrectomy on Sprague-Dawley rats prior to acute hemodilution of 50% of their estimated blood volume with hydroxyethyl starch (n=6). Heart rate, mean arterial pressure and brain microvascular pO_2 (OxyLED, Oxyphor G4) were measured continuously. Arterial blood gases, and cooximetry samples were taken at baseline, 10, 30 and 90 minutes post-hemodilution. Results were tested for normality and analysis performed by two-way ANOVA with $p<0.05$ as significant.

Results:

Heart rate (sham: 361±20 bpm, nephrectomy: 301±33 bpm, p=0.005) and brain microvascular pO_2 (sham: 28.5±8.9 mmHg, nephrectomy: 21.2±5.1 mmHg, p=0.057) were lower at baseline in nephrectomised rats. Following hemodilution, microvascular brain pO_2 ($p_{Br}O_2$) of nephrectomised rats decreased significantly relative to baseline and sham $p_{Br}O_2$ values (sham: 27.3±11.2 mmHg, nephrectomy: 14.2±7.7 mmHg, p=0.031). The difference resolved after 40 minutes. A small reduction in hemoglobin concentration (sham: 61.4±5.1 g/L, nephrectomy: 46.3±4.4 g/L, $p<0.001$), blood oxygen saturation (sham: 96.1±0.9 %, nephrectomy: 98.2±1.4 %, p=0.011) and CaO_2 (sham: 82.1±6.5 mL/mL, nephrectomy 63.4±5.4 mL/mL, $p<0.001$) was observed in nephrectomised rats, which may have contributed to this response.

Discussion:

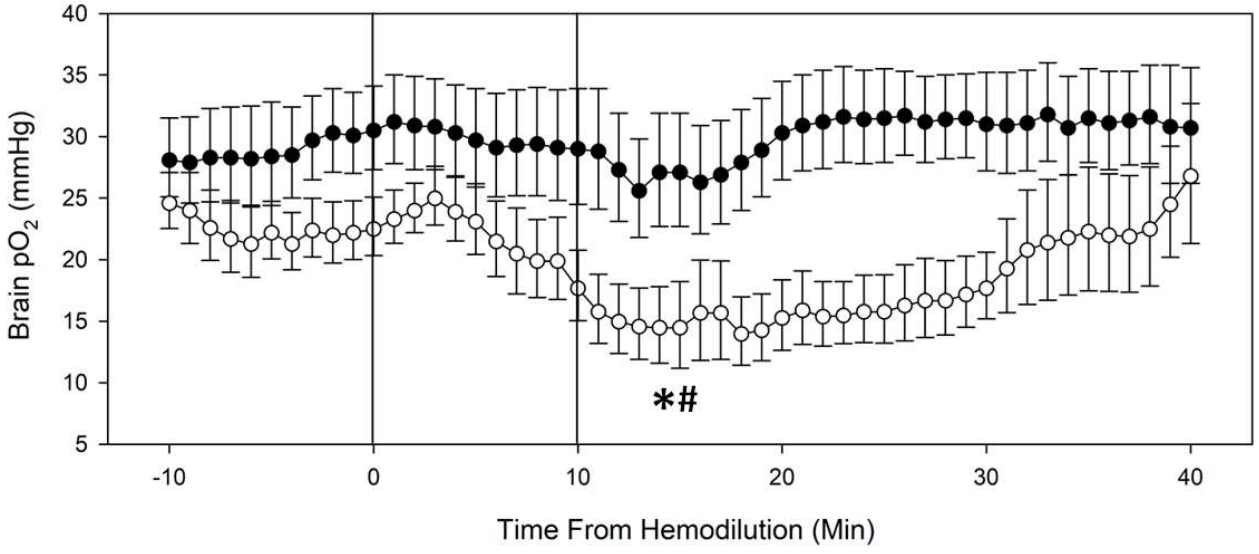
Bilateral nephrectomy resulted in changes in baseline physiology and resulted in an acute reduction in brain microvascular pO_2 after acute hemodilution supporting the hypothesis that the kidney contributes to maintain brain oxygenation during acute anemia. The kidney's capacity as an oxygen sensor [4,5] may contribute to this function. Further assessment of physiological parameters, including cardiac output and cerebral blood flow and

systemic biomarkers of tissue hypoxia, may help elucidate the mechanism(s). CAS-CARF support.

References:

1. Karkouti, K., Wijeysundera, D. N., & Beattie, W. S. (2008). Risk associated with preoperative anemia in cardiac surgery: A multicenter cohort study. *Circulation*, *117*(4), 478–484. https://doi.org/10.1161/CIRCULATIONAHA.107.718353
2. Musallam, K. M., Tamim, H. M., Richards, T., Spahn, D. R., Rosendaal, F. R., Habbal, A., Khreiss, M., Dahdaleh, F. S., Khavandi, K., Sfeir, P. M., Soweid, A., Hoballah, J. J., Taher, A. T., & Jamali, F. R. (2011). Preoperative anaemia and postoperative outcomes in non-cardiac surgery: a retrospective cohort study. *Lancet (London, England)*, *378*(9800), 1396–1407. https://doi.org/10.1016/S0140-6736(11)61381-0
3. Ashes, C., Judelman, S., Wijeysundera, D. N., Tait, G., Mazer, C. D., Hare, G. M. T., & Beattie, W. S. (2013). Selective β1-Antagonism with Bisoprolol Is Associated with Fewer Postoperative Strokes than Atenolol or Metoprolol A Single-center Cohort Study of 44,092 Consecutive Patients. *Anesthesiology*, *119*(4), 777–787. https://doi.org/10.1097/ALN.0B013E3182A17F12
4. Abrahamson, J. R., Read, A., Chin, K., Mistry, N., Joo, H., Desjardins, J. F., Liu, E., Thai, K., Wilson, D. F., Vinogradov, S. A., Maynes, J. T., Gilbert, R. E., Connelly, K. A., Baker, A. J., David Mazer, C., & Hare, G. M. T. (2020). Renal tissue PO2 sensing during acute hemodilution is dependent on the diluent. *American Journal of Physiology - Regulatory Integrative and Comparative Physiology*, *318*(4), R799–R812. https://doi.org/10.1152/ajpregu.00323.2019
5. Chin, K., Cazorla-Bak, M. P., Liu, E., Nghiem, L., Zhang, Y., Yu, J., Wilson, D. F., Vinogradov, S. A., Gilbert, R. E., Connelly, K. A., Evans, R. G., Baker, A. J., David Mazer, C., & Hare, G. M. T. (2021). Renal microvascular oxygen tension during hyperoxia and acute hemodilution assessed by phosphorescence quenching and excitation with blue and red light. *Canadian Journal of Anesthesia*, *68*(2), 214–225. https://doi.org/10.1007/s12630-020-01848-5

Figure 1:



#; p<0.05 vs Control. *; p<0.05 vs Baseline.