# Impact of Hypothermic and Normothermic Machine Perfusion on renal resistance, vascular flow and graft inflammatory state in an experimental model of DCD

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## Background

Kidney transplantation is currently the standard treatment for patients with end-stage renal disease, unfortunately, the shortage of available donor kidneys represents an important limitation that forced to accept marginal, higher-risk organs from circulatory death (DCD) donors and expanded criteria donors. Recently, the use of hypothermic (HMP) and normothermic (NMP) perfusion machines is an important strategy to improve graft quality, thereby to increase renal function and survival.

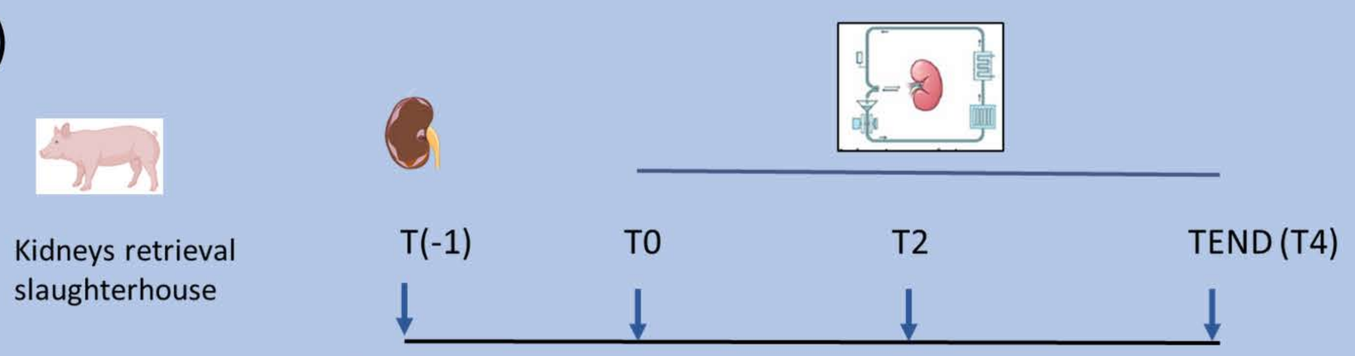
## METHODS

In an experimental model of donation in cardiac death (DCD), after 60 minutes of warm ischemia, porcine kidneys were retrieved in anatomical blocks in a certified and standardized slaughter facility (UNI-En ISO 9001) and subjected to Standard Cold Storage overnight (SCS ) (**Fig 1**). The oxygenated hypothermic and normothermic renal perfusion were carried out using the innovative PerLife system (PerKidney, Aferetica) with a pressure of 75 mmHg, oxygenation 1100 ml/min and a duration of 4h. Gradual increase of temperature was possible in normothermic treatment ranging from 8 °C to 32 °C. The perfused organs biopsies were compared to organs stored on ice (SCS). In vitro analysis, endothelial cells exposed to $H_2O_2$, C5a were analyzed by cell proliferation assay, qPCR, Western blot and FACS analysis.

## RESULTS

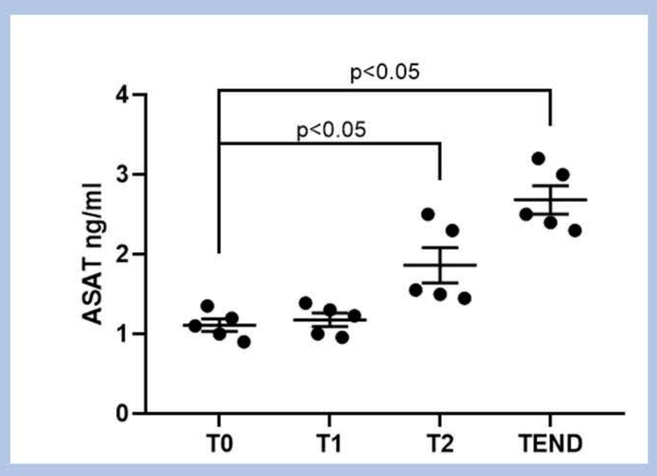
Compared with the beginning of treatment (T0), resistances and flows improved in both HMP and NMP perfused kidneys groups.
ELISA data on perfusates show a significant reduction of levels of MCP-1, TNFα, ICAM, VCAM and the renal injury markers ASAT (**Fig 2**) and LDH compared to T0 ($p<0,05$), the reduction was observed both HMP and NMP treatments. In the SCS group, by histological staining (eosin and hematoxylin and PAS stainings) the tubules appear dilated, the interstitium with infiltrate, the floccule detached from the Bowman capsule. HMP and NMP treatment reduced tubular necrosis compared to SCS, particularly NMP treatment appeared more efficient compared to HMP ($p<0,05$). Endothelial cells after H2O2 and C5a exposition and tissues from SCS organs showed increased IL-6 and Endothelin-1 gene expression, indicating the acquirement of a pro-inflammatory state and vasoconstriction.

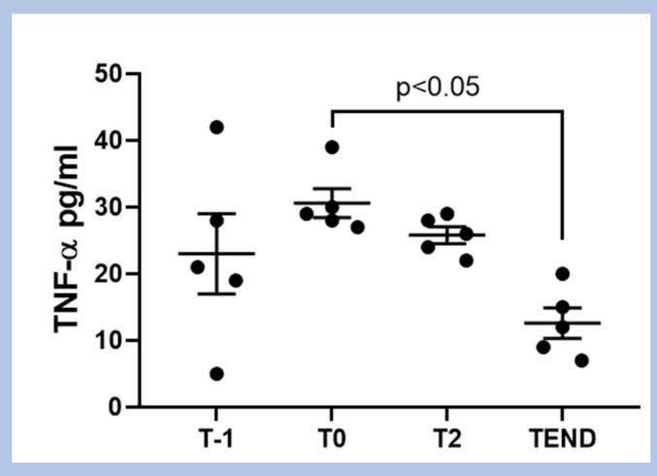
1)




| Resistance/Flow | | x | x | x |
|---|---|---|---|---|
| Biopsy | x | x | x | x |
| Perfusate analysis | x | x | x | x |

2)




## CONCLUSION

HMP and NMP treatments induced a reduction in the gene expression of IL-6 and Endothelin-1 compared to SCS renal tissue. The use of HMP and NMP could counteract tissue damage, and inflammation induced by the ischemia-reperfusion and increase the possibility of using marginal organs.