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Organ preservation: which temperature for which organ?

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In 1954, Joseph Murray performed the first successful human organ transplant from a live kidney donor, Ronald Herrick, into the donor's twin brother, Richard. Since no form of organ preservation was available, the surgeries took place simultaneously in two operating rooms. In this way, the kidney damage subsequent to the lack of blood supply before the vascular anastomoses between Richard's vessels and Ronald's kidney were confectioned, was reduced to a minimum.[1] Richard recovered well and died in 1962 as a result of the recurrence of his original nephritis disease.

Seventy years after Murray's pioneering surgery, optimal graft preservation prior to implantation into the recipient's body remains one of the major challenges in transplantation surgery. The primary graft function and its long-term outcomes are dependent on ischaemia–reperfusion injury (IRI),[2] with considerable parenchymal damage occurring during the preservation period after retrieval and before implantation. There is evidence that different organs have different resistance thresholds to the ischaemic insult and these thresholds could be affected by the preservation modality.[3,4]

The three main organ preservation techniques include static cold storage (SCS), hypothermic machine perfusion (HMP) and normothermic machine perfusion (NMP); to date, SCS remains the most common preservation modality because of its simplicity and lower cost, despite growing evidence of a higher risk of subsequent transplant damage.[5]

Literature has shown that organs retrieved from extended criteria donors and donors after cardiocirculatory death are more susceptible to IRI when compared with standard donors.[6,7] Thus, to keep expanding the donor pool with marginal organs, it is paramount to tailor the preservation modality to the characteristics of the individual graft.[8]

Ex situ organ perfusion was introduced in the early 1900s by Charles Lindbergh and Alexis Carrel, who developed the first machine perfusion to preserve animal organs.[9] Yet, it was not until 1967, when Belzer transplanted a deceased donor kidney after 17 hours of preservation, that

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HMP was clinically used.[10] The graft worked immediately post-transplantation.

What is the rationale to cool the organ down before implantation? Is there a temperature paradigm? We know that hypothermia slows down cell metabolism, thus reducing oxygen requirements during the ischaemic period outside the human body.[11] Yet, there is no evidence for the gold standard temperature for human grafts. With this idea in mind, 20 years ago, we copyrighted a device that allowed the temperature to be modified according to the human graft that was being transported.[12] This was a compact machine that was able to switch and maintain a set temperature between –20°C and +37°C, to allow the storage of different organs and tissues being transported from the donor's hospital to the recipient's site.

Is maintaining organs at 37°C, the human body temperature, a possible way forward? The basic principle of NMP for organ preservation is to minimize the deleterious effects of ischaemia and anoxia while the organ is outside the human body. The hypothermic setting slows down cell metabolism and reduces the demand for oxygen, but it does not prevent the chemical processes that cause the ischaemic injury during the preservation period.[13,14] Despite the possibility of delivering oxygen during HMP by using hypothermic oxygenated machine perfusion, as demonstrated in clinical studies,[15] NMP seems to provide, in addition of oxygen, a more physiological platform to repair marginal organs by delivering therapeutics in direct contact with the organ blood supply, thus avoiding most of the complications associated with systemic delivery.[16]

In conclusion, one size might not fit all. It remains unclear which temperature setting is preferable to another for optimal organ preservation. There is no consensus on what the optimal temperature is for different organs and their intrinsic characteristics, but the preservation modality might be tailored on a case-by-case basis. Current research is directed at developing different techniques to improve practices, assessment and reconditioning of organ viability pre-transplantation.

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