

Kidneys preservation before transplantation

Mini-review

Any method of preservation has the objective to maintain the organ in the best conditions during the period between the retrieval and the transplant, lowering the ischemia/reperfusion injury. Ideal preservation system should allow extending the ischemia time of the graft, improving its function and enabling the use of organs which initially were considered not suitable for transplant. Static storage with hypothermic solution (perfusing the organ through a catheter positioned in the renal artery with a cold storing solution immediately after the retrieval, leaving the graft inside a sterile container covered with ice with a temperature within 0°C and 4°C) is still considered the gold standard for kidneys preservation.¹ Plenty of perfusion solutions exist, with different chemical-physical characteristics; those which mostly have been used for kidneys preservation are Belzer UW® *Cold Storage Solution* (UW Solution) and *Celsior® Genzyme*. Comparative trials among these perfusion solutions have not showed advantages in using the first or the second, in particular any difference in terms of delay graft function (DGF) and graft and patient survival.²⁻⁵ Despite recent studies have showed that other preservation methods allow better results after transplantation, the simplicity (application capacity even by non-expert personnel) and the economicity (few devices needed) of the static storage still justify its widespread utilization.⁶

Because of the shortage of the number of the donors, kidney transplants are performed often and often using grafts coming from marginal donors (ECD, extended criteria donors).⁷ As these grafts are more susceptible to the ischemia injury,⁸ these organs have higher rate of post-transplant complications, in particular DGF and primary non function (PNF).⁸⁻¹² Strategies to improve the outcome of transplants performed using grafts coming from “non-ideal” donors are therefore investigated. Some authors showed that hypothermic pulsatile perfusion significantly reduces the risk of DGF compared to the classic static storage.¹³⁻¹⁵ Despite it is a significant difference, the rate of DGF observed using the pulsatile perfusion is not absolutely much inferior than that one observed in the static storage. This type of perfusion is ensured positioning the kidney after the retrieval inside a machine (*LifePort Kidney Transporter®-Organ Recovery System*), which continually perfuses the kidney with an hypothermic solution with a pulsatile pressure through a peristaltic pump within a closed circulation, measuring peristaltic pulse rate, solution temperature, mean systolic and diastolic pressures, real time flow and flow resistance. Hypothermic pulsatile perfusion would have the possibility to provide to the tissues higher level of ATP and to perfuse continually microcirculation, eliminating in this way waste products.

Other strategies to reduce the ischemia/reperfusion and to improve the function of the graft are the normal temperature (or sub-normal) preservation systems. The normothermic perfusion (EVNP, *ex vivo* normothermic perfusion) and the resurrection techniques have already been used for heart and lung transplantation,¹⁶⁻¹⁸ but just recently they have been applied also to the kidney transplantation.¹⁹ In an experimental porcine model of EVNP kidneys undergone to this treatment had lower level flow resistance, better homeostasis of the acid-basis equilibria, high level of oxygen consumption, lower tubular

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injury, high level of IL-6 and of heat shock protein 70, compared to control group kidneys (static storage), with no differences in inflammatory cytokines (IL-1 β , IL-8, TNF- α) expression levels or in kidney function (creatinine clearance).²⁰ Other clinical studies show that EVNP reduces rates of DGF of transplants performed using grafts coming from ECD, without modifying outcome in the long run (graft and patient survival).²¹ Actual data from the literature report single centers experiences, with a limited number of treated patients, and no multicentric study with a wide sample study is available.

The last research sector to improve the function of the kidney to transplant concerns the hypothermic oxygenated perfusion. The use of oxygenated solution would have the goal to provide oxygen to the organ, so to support the re-synthesis of ATP, delaying the formation of many toxic intracellular substances. However high concentrations of oxygen increase the production of reactive oxygen species (ROS), which cause further oxidative stress and tissue injury.^{22,23} The oxygenation of the solution and of the organ can be effectuated through a lot of techniques: adding oxygen to the perfusion solutions (static or dynamic), increasing the atmospheric pressure (hyperbaric oxygenation, static or dynamic), using oxygen artificial transporters. We still don't know if organs oxygenation could offer advantages to the outcome after kidney transplant,²⁴ several trials which try to answer to this query are ongoing. Despite technological progress drive the research and the clinical practice to the application of new strategies, the majority of the Transplant Centers still mostly uses static storage. Pulsatile perfusion has allowed to reduce some short term outcomes, without modifying graft or patient survival and without allowing the use of kidneys initially considered not suitable for transplant. Kidneys oxygenation (normothermic or hypothermic) would provide good future perspectives, able to improve sensitively short and long term outcomes and to increase the pool of grafts to destined to transplantation.

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Conflict of interest

The author declares no conflict of interest.

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