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The narrow window in solid organ transplantation is widening; Does "Golden Time" still apply?

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Abbreviations

WHO, World health organization; OLT, Orthotopic liver transplantation; UW solution, University of Wisconsin solution

Liver is the largest internal organ in the body and has a crucial role in metabolic homeostasis. This organ is responsible for many essential metabolic, regulatory, exocrine and endocrine functions. According to world health organization (WHO), end-stage liver diseases are the 12th cause of mortality and their incidence is increasing globally [1]. Orthotopic liver transplantation (OLT) is the "gold standard" and the only treatment for end-stage liver diseases. The success of OLT has increased owing to the improved immunosuppressive regimens, updated surgical techniques, and more advanced donor-recipient pairing methods [2]. The OLT is still facing several obstacles, including the shortage of eligible donors, post-operational complications, high hospitalization costs, and the need for lifelong immunosuppressive therapy [3]. Another major limitation in organ transplantation is the narrow window of time for transporting and implanting the donor's graft to the host. Usually, this window is less than 12 hours. Optimization of organ preservation protocols to deliver donated organs of high quality via a network of organ exchange and matching the recipient to the best available organ, capable of rapid resumption of function, is very important [4]. Working on organ preservation started in the 1960s. The pioneering work by Collins and his colleagues in 1969 led to the development of a solution that could mimic the intracellular electrolyte balance of the mammalian cells. That was the first notable attempt to preserve an organ based on understanding the ongoing changes during cooling in cells [4]. In the late 1980s, researchers introduced University of Wisconsin (UW) solution which changed the organ transplantation surgery from emergent to a semi-emergent method [5-7]. In the 1960s, machine perfusion became a part of clinical practice, aiming to extend the preservation time for organ transplantation [8]. In the past decade, significant progress in using machine perfusion for organ preservation has been recorded. The main concept behind machine perfusion is supplying dynamic reconditioning and repair through restoring blood circulation after cannulating the donated organ and providing continuous perfusion through a pump. This machine can enrich the media and add oxygen, nutrients, and therapeutic agents in order to support the donated organ [9]. Ex vivo machine perfusion can be utilized at different temperatures; hypothermia, normothermia, and subnormothermia.

No significant evidence exists for choosing one solution over the others for perfusion [9]. Clinical research showed significant superiority of using machine perfusion in kidney transplantation over static cold storage [9]. The use of machine perfusion in the pancreas is still in the pre-clinical and experimental phase and may cause edema in the pancreas due to its low-flow rate [9]. In May 2021, Pierre-Alain Clavien and Mark W. Tibbitt, using an ex-situ normothermic machine perfusion managed to preserve a liver for transplantation for three days. The liver in question was declined from other transplantation centers because of the presence of chronic abdominal abscesses and a tumor of unclear origin. After finding that the tumor is benign and eliminating multidrug-resistant bacteria by using high doses of antibiotics; the liver was transplanted successfully into a 62 years old patient. The clinical success is that the transplanted liver had normal function with minimum reperfusion injury that resulted in a standard quality of life for the patient after the transplantation during 1-year follow-up that only needed a minimal immunosuppressive regimen. This clinical success promises an extended time window of up to 10 days for organ transplantation, which can change the transplantation process from an urgent surgery to an elective procedure with a more efficient algorithm in pairing and matching donated organs and recipients [10]. This breakthrough can make a remarkable change in other solid organ transplantations.

Declarations

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Authors' Contributions

P.D. drafted the manuscript, M.V. conceived the manuscript, and S.N. and M.V. reviewed and approved the manuscript.

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