



## Pulsatile Preservation in Renal Transplantation

M.L. Henry

**A** KEY factor determining the quality of a transplanted organ is the quality of its preservation. Allograft injury during preservation can affect early outcome. Immediate function of a transplanted organ is related to many factors; however, preservation is arguably the most important. Studies have shown poorer 1-year graft survival in recipients of kidneys requiring dialysis posttransplantation, compared with those having good early graft function.<sup>1-5</sup> One-year graft survival can be as much as a 20% poorer in those with delayed graft function (DGF). If the incidence of DGF can be positively affected by pulsatile preservation, the graft survival may be directly affected. Because of its unique properties (pulsatile flow) and the ability to make objective measurements of flow and pressure, it also affords an opportunity to make decisions about whether a specific organ should be used based on the characteristics of the organ during preservation. The use of marginal and non-heart-beating donors has driven several centers to the use of pulsatile preservation, to evaluate and predict the usefulness of those organs prior to transplantation.

### Advantages and Disadvantages

There are several advantages of pulsatile perfusion versus simple cold storage. These include (1) a lower incidence of DGF, (2) better preservation over longer periods of time (especially at >24), (3) the ability to monitor flow rates and pressures and thus monitor intrarenal resistance during perfusion, (4) decreased intrarenal vasospasm, (5) the ability to provide metabolic support during perfusion, and (6) the potential to manipulate flow pharmacologically during perfusion. Potential disadvantages include (1) increased costs, (2) endothelial injury, and (3) equipment failure. The advantages of simple cold storage are that it is logistically easier, easier to share organs, and less demanding of highly trained personnel.

### Preservation Solutions

Improvements in preservation solutions have occurred in recent years. Cryoprecipitated plasma was used widely in the early days of pulsatile preservation. Batch-to-batch variability, complex preparation techniques, and the potential risk of disease transmission, caused it to fall out of favor. Other solutions were used, such as human serum albumin, plasma protein fraction, and silica gel fraction. The Belzer perfusate was developed at the University of

Wisconsin and has gained favor in many US centers for pulsatile preservation. It has been used in two forms, differing primarily only in the colloid fraction. The first was an albumin-based solution, but the most recent formulation is pentastarch based. Clinical outcome has been excellent with both forms of the Belzer perfusate; however, recent studies have demonstrated that the pentastarch-based mixture provides a lower incidence of DGF.<sup>6,7</sup>

### Outcomes

Conclusions regarding studies directly comparing the outcome of simple cold storage versus pulsatile perfusion should be made with caution. Small prospective studies have been done,<sup>8-14</sup> and other retrospective investigations are also available for review.<sup>15-18</sup> Studies that demonstrate differences in early function between the two methods of preservation tend to favor pulsatile perfusion. Of the seven prospective randomized trials, four demonstrated significantly improved immediate function with pulsatile preservation, and three showed statistically insignificant differences favoring simple cold storage. The two studies with the largest patient populations are neither prospective nor randomized, but each demonstrates at least a 10% advantage in improved early function with pulsatile perfusion.<sup>7,16</sup> In an interesting description of the survey results of centers using pulsatile perfusion, Light et al<sup>18</sup> identified eight centers that routinely use monitored pulsatile preservation; their mean incidence of immediate graft function following renal transplantation was 95%, with a mean duration of preservation of 24 hours. These results should be compared with the reported incidence of immediate function of 75% nationally.<sup>19</sup>

The dynamic quality of pulsatile preservation provides information that is not available with simple cold storage. As a result of the circulating fluids and the apparatus that contains it, the flow through each kidney can be measured. Pulsatile pressures are routinely measured, and mean pulsatile pressures are calculated. By using these two parameters, intrarenal resistance can be calculated (resistance = flow/mean pressure). Several observations have been made

---

From the Department of Surgery, Ohio State University, Columbus, Ohio, USA.

Address reprint requests to Mitchell L. Henry, MD, The Ohio State University, Department of Surgery, Division of Transplantation, 1654 Upham Drive, #345, Columbus, OH 43210-1250.

from these measurements. First, kidneys procured and placed on the pulsatile preservation machine routinely "dilate" (decreased resistance) during the first few hours of preservation. In addition, pharmacologic manipulation of the organs with vasodilators can improve the flow characteristics in these organs. This manipulation allows improved perfusion and better access of the preservation solution to the microvasculature. Ongoing perfusion also dilutes the potentially harmful products of the remaining cellular metabolism, found even in the cold-preserved organ. The outcome of transplanted kidneys as a function of these perfusion characteristics has been reported.<sup>20</sup> It was demonstrated that kidneys with poor perfusion properties (ie, high intrarenal resistance) had a high incidence of DGF and primary non-function. Tesi et al<sup>21</sup> reviewed the outcome of "imported" kidneys previously cold stored and secondarily pump perfused upon arrival at our center. They again found that the flow characteristics during pulsatile preservation can predict which kidneys are likely to perform poorly posttransplantation. At present, with an ever-increasing number of patients on the waiting list and a relatively static organ supply, many centers have decided deliberately to utilize older and more "marginal" donors. This approach has been used in Japan in kidneys procured from non-heart beating donors.<sup>14</sup> Machine preservation, as described here, can be an important determinant of the likelihood that a given pair of kidneys will be worth transplanting. Studies that have compared the length of perfusion have uniformly found that immediate function was improved in the pulsatile perfusion group under conditions of prolonged preservation.<sup>7,13,16,22</sup>

### Costs

The increased cost associated with its use is one purported disadvantage of pulsatile preservation. There are initial costs of the mechanical equipment, as well as the costs of disposables (eg, perfusion cassettes) and technician time. These expenses, on the surface, can appear to add significantly to the cost of pulsatile preservation over that of simple cold storage. However, if the quality of the organ, as a function of the presence or absence of DGF, is better in grafts preserved by pump perfusion, considerable cost savings can be realized. These savings are represented not only by the decreased hospital costs associated with immediate function but also by the fact that there are fewer graft losses over both the short and long term.

With the reduced incidence of DGF associated with pulsatile preservation, it is apparent that these large hospital cost savings outweigh the increased costs of this method of preservation. One of the problems with this equation, however, is that the organ procurement organizations incur the preservation costs, while the recipient centers realize the cost savings.

### CONCLUSIONS

The interest in pulsatile preservation is increasing. A very low incidence of DGF can be demonstrated in centers that

routinely use this form of preservation. Newer formulations of the preservation solutions have been shown to be superior to those previously utilized. Because of the nature of the process of pulsatile preservation, resistance can be calculated and followed during the course of preservation. This has allowed for choices regarding the use of a particular organ, especially for those undergoing prolonged perfusion or those from marginal and non-heart-beating donors. Initial expenses of preservation are increased with this method, due primarily to equipment and personnel costs. However, the improved immediate function rates and the decreased need for dialysis can lead to a significant reduction in the overall costs of transplantation.

### REFERENCES

1. Sanfilippo F, Vaughn WK, Spees EK, et al: *Transplantation* 38:643, 1984
2. Halloran PF, Aprile MA, Farewell V, et al: *Transplantation* 46:223, 1988
3. Lim EC, Terasaki PI: In Terasaki P, Cecka JM (eds): *Clinical Transplants 1991*. Los Angeles, Calif: UCLA Tissue Typing Laboratory; 1992, p
4. Ferguson RM, et al: *Clin Transplantation* 2:285, 1988
5. Cecka JM, Terasaki PI: In Terasaki P (eds): *Clinical Transplants 1990*. Los Angeles, Calif: UCLA Tissue Typing Laboratory; 1991, p
6. Hoffman RM, Stratta RJ, D'Alessandro AM, et al: *Transplantation* 47:32, 1989
7. Gruessner RW, Nakhleh R, Tzardis P, et al: *Transplantation* 56:1053, 1993
8. Alijani MR, Cutler JA, DelValle CJ, et al: *Transplantation* 40:659, 1985
9. Merion RM, Oh HK, Port FK, et al: *Transplantation* 50:230, 1990
10. Halloran P, Aprile M: *Transplantation* 43:827, 1987
11. Mendez R, Mendez RG, Koussa N, et al: *Transplant Proc* 19:2047, 1987
12. Heil JE, Canafax DM, Sutherland DER, et al: *Transplant Proc* 19:2046, 1987
13. Veller MG, Botha JR, Britz RS, et al: *Clin Transplantation* 8:97, 1994
14. Matsuno N, Sakurai E, Tamaki I, et al: *Transplantation* 57:29, 1994
15. Barber WH, Laskow DA, Deierhoi MH, et al: *Transplant Proc* 23:2394, 1991
16. Koyama H, Cecka JM, Terasaki PI: *Clin Transplantation* 7:199, 1993
17. Johnson CP, Roza AM, Adams MB: *Transplant Proc* 22:385, 1990
19. Cecka JM, Terasaki PI: In Terasaki PI and Cecka JM (eds): *Clinical Transplants 1994*. Los Angeles, Calif: UCLA Tissue Typing Laboratory; 1995, p
20. Henry ML, Sommer BG, Ferguson RM: *Transplantation* 45:73, 1988
21. Tesi RJ, Elkhaymas EA, Davies EA, et al: *Clin Transplantation* 8:134, 1994
22. Koning OHJ, Van Bockel JH, Van der Woude FJ, et al: *Transplant Proc* 27:752, 1995