ORIGINAL ARTICLE

Hypothermia or Machine Perfusion in Kidney Donors

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ABSTRACT

BACKGROUND

Therapeutic hypothermia in brain-dead organ donors has been shown to reduce delayed graft function in kidney recipients after transplantation. Data are needed on the effect of hypothermia as compared with machine perfusion on outcomes after kidney transplantation.

METHODS

At six organ-procurement facilities in the United States, we randomly assigned brain-dead kidney donors to undergo therapeutic hypothermia (hypothermia group), ex situ kidney hypothermic machine perfusion (machine-perfusion group), or both (combination-therapy group). The primary outcome was delayed graft function in the kidney transplant recipients (defined as the initiation of dialysis during the first 7 days after transplantation). We also evaluated whether hypothermia alone was noninferior to machine perfusion alone and whether the combination of both methods was superior to each of the individual therapies. Secondary outcomes included graft survival at 1 year after transplantation.

RESULTS

From 725 enrolled donors, 1349 kidneys were transplanted: 359 kidneys in the hypothermia group, 511 in the machine-perfusion group, and 479 in the combined-therapy group. Delayed graft function occurred in 109 patients (30%) in the hypothermia group, in 99 patients (19%) in the machine-perfusion group, and in 103 patients (22%) in the combination-therapy group. Adjusted risk ratios for delayed graft function were 1.72 (95% confidence interval [CI], 1.35 to 2.17) for hypothermia as compared with machine perfusion, 1.57 (95% CI, 1.26 to 1.96) for hypothermia as compared with combination therapy, and 1.09 (95% CI, 0.85 to 1.40) for combination therapy as compared with machine perfusion. At 1 year, the frequency of graft survival was similar in the three groups. A total of 10 adverse events were reported, including cardiovascular instability in 9 donors and organ loss in 1 donor owing to perfusion malfunction.

CONCLUSIONS

Among brain-dead organ donors, therapeutic hypothermia was inferior to machine perfusion of the kidney in reducing delayed graft function after transplantation. The combination of hypothermia and machine perfusion did not provide additional protection. (Funded by Arnold Ventures; ClinicalTrials.gov number, NCT02525510.)

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Among kidney transplant recipients, the relative risk of delayed graft function was reported to be 38% lower with the use of therapeutic hypothermia (34 to 35°C) than the use of normothermia in brain-dead organ donors. The benefit was most pronounced among high-risk donors.[1]

In a trial conducted by the Eurotransplant International Foundation in 2009,[2] the protective effect of ex situ kidney hypothermic machine perfusion as compared with static cold storage was similar to that reported in the above-mentioned hypothermia trial (odds ratio, 0.57 and 0.62, respectively). However, machine-perfusion logistics are complex, and the cost of machine perfusion can be substantial for organ-procurement organizations and transplant centers. Machine perfusion of kidneys from donors has been increasingly adopted by many centers in the United States even though the clinical and cost effects of this intervention remain uncertain.

We performed a pragmatic, adaptive, prospective, randomized trial to assess whether targeted mild hypothermia is as effective as machine perfusion of kidneys obtained from brain-dead donors who were identified as being eligible for machine perfusion of their kidneys. We also sought to determine whether the combination of the two strategies would be superior to either one alone. We hypothesized that a finding that mild hypothermia was noninferior to machine perfusion would lead to considerable cost savings and streamlined logistics.[3]

Methods

Trial Design

The trial was conducted between August 10, 2017, and May 21, 2020, in seven states: Arizona, Colorado, Minnesota, North Dakota, Oregon, South Dakota, and Texas; organ assignments were managed by six organ-procurement organizations in their respective donation service areas. The date of the last follow-up to assess recipients' 1-year kidney function was June 14, 2021. Brain-dead donors who had kidneys that were eligible for machine perfusion were clinically managed by each organ-procurement organization according to their guidelines, in accord with the donor management goals of the United Network for Organ Sharing.[4] We determined eligibility for machine perfusion of kidneys on the basis of the protocol at each participating organ-procurement organization according to a pragmatic trial approach.[4,5] The target temperature for mild hypothermia was 34 to 35°C.

At four of the six organ-procurement organizations, eligibility for machine perfusion is determined by the presence of indications of inferior organ quality (i.e., criteria for expanded donors or a high score on the Kidney Donor Profile Index). The other two organ-procurement organizations used machine perfusion for all kidneys. Although kidney donors who were eligible for either mild hypothermia or machine perfusion were enrolled under the same overall protocol, the donors underwent separate randomizations in the two groups; data collection in the mild-hypothermia group is ongoing. Here, we report only the results with respect to donors of kidneys that were eligible for machine perfusion.

A Quick Take is available at NEJM.org

Oversight

The trial was funded by Arnold Ventures, a philanthropic foundation that invests in multiple fields of research, including medical issues. The trial was approved by the institutional review board at the University of California, San Francisco.

All the authors participated in the design and implementation of the trial and collected and analyzed the data. The first and last authors wrote the first draft of the manuscript and made the decision to submit the manuscript for publication; all the authors contributed to the subsequent versions. All the authors vouch for the accuracy and completeness of the data and for the fidelity of the trial to the protocol, available with the full text of this article at NEJM.org. Access to the data was not restricted by confidentiality agreements.

Donors

All the kidneys that were used in the trial were obtained from brain-dead organ donors who were at least 18 years of age and who had provided research authorization, regardless of whether their donation was based on standard or expanded criteria and regardless of sex or ethnic background. The condition of all donors needed to be hemodynamically stable with the receipt of low-dose vasopressors and with a mean arterial pressure of more than 60 mm Hg. Coagulopathy and electrolyte abnormalities needed to have been corrected. Key exclusion criteria

were donation after cardiac death, end-stage kidney disease, or a history of dialysis during terminal hospitalization. Additional details are provided in the Supplementary Appendix, available at NEJM.org.

RANDOMIZATION, TRIAL INTERVENTION, AND DATA COLLECTION

After research authorization had been confirmed and enrollment criteria had been met (including a temperature of >36°C), brain-dead donors who were eligible for machine perfusion were assigned by computer-generated block randomization to normothermia with subsequent ex situ hypothermic, nonoxygenated machine perfusion of both kidneys, therapeutic hypothermia (34 to 35°C) in the donor with perfusion of the right kidney, or donor hypothermia and machine perfusion of the left kidney. Kidneys were randomly assigned in a 1:1:1 ratio to machine perfusion only, hypothermia only, or a combination of the two methods (see randomization plan 1 in Fig. S1 in the Supplementary Appendix). Randomization was stratified according to organ-procurement organization, standard or expanded donor criteria (on the basis of established definitions[6]), and the receipt of therapeutic hypothermia before death. The randomization plan and trial protocol were adjusted after the first interim analysis according to prespecified stopping criteria (randomization plan 2 in Fig. S1). Temperature management was handled according to a trial protocol that was applied by organ-procurement coordinators, as was reported previously (Table S1).[1]

Details regarding the collection process are provided in the Supplementary Appendix, along with information regarding the organ-procurement organizations, donor data, the definition of the Kidney Donor Profile Index (as determined by the Scientific Registry of Transplant Recipients),[7] and recipient-specific data to which the trial data were linked.

OUTCOMES

The primary outcome was delayed graft function, which was defined as the initiation of dialysis in the kidney recipient during the first 7 days after transplantation. For each kidney recipient, a primary-outcome event was determined by personnel at the center where the organ had been transplanted. These data were reported to the United Network for Organ Sharing as a part of the routine submission process. Adverse events were defined as events that had led to active intervention to correct a physiological derangement.

Secondary outcome measures were allograft survival at 1 year and the number of all other solid organs that had been transplanted from each donor. We also evaluated whether hypothermia alone was noninferior to machine perfusion and whether the combination of both strategies was superior to each of the individual methods.

STATISTICAL ANALYSIS

We evaluated the statistical power of the trial and the type I error by simulation across a range of scenarios to determine the sample size. The trial included prespecified interim analyses to determine the inferiority of any of the three treatments. Interim analyses were performed according to an O'Brien–Fleming stopping boundary, which accounted for the multiple interim analyses. We used Holm's adjustment to account for the pairwise comparisons of the three groups. The total two-sided alpha level was 5% across the interim and final analyses. The alpha-spending function accounts for the multiple interim analyses. The first interim analysis spent 0.0028 of the total 0.05 alpha level. Table S2 shows the timing of the interim analyses, the nominal P values for success or failure that were required at each interim analysis, and the alpha that was spent at each analysis.

The primary analysis was performed according to the intention-to-treat principle and included all transplanted kidneys for which the status was known regarding the presence or absence of delayed graft function. We used a logistic generalized-estimating-equation regression model with a compound symmetric (i.e., exchangeable) correlation structure to account for the hierarchical nature of the data (one or two kidneys transplanted from a single donor). The model included terms for the randomly assigned treatment group, organ-procurement organization, standard or expanded donor criteria, creatinine level at enrollment, donor age, and the duration of cold-ischemia time for the transplanted kidney. (The cold-ischemia time is defined as the interval after the organ has been removed from the donor until it is revascularized in the recipient.)

The primary outcome was defined as 1 in the presence of delayed graft function and as 0 in the absence of delayed graft function. As a result, an estimated odds ratio of less than 1 represented a favorable treatment effect, and an odds ratio of 1 or more represented an unfavorable treatment effect. The primary objective was to determine whether hypothermia alone was noninferior to machine perfusion alone in the prevention of delayed graft function in the kidney recipients. The noninferiority of hypothermia was determined if the upper boundary of the 95% confidence interval fell below 1.4, a margin that was based on what was considered to be a clinically meaningful difference according to common practice. The handling of missing covariate data is described in Table S3.

All data analyses were performed with the use of R software, version 4.1.0. Full details regarding the statistical analysis plan, including interim analyses, adaptive stopping rules, and governance of the trial by an independent data and safety monitoring board, are provided in the Supplementary Appendix.

RESULTS

TRIAL PROCEDURES AND INTERIM ANALYSES

On the basis of a recommendation from the data and safety monitoring board, the trial was terminated early for expected futility in determining the superiority of a combination of hypothermia and machine perfusion as compared with machine perfusion alone. Of the 3087 organ donors with research authorization who had undergone screening, 2177 were excluded for a variety of reasons, including donation after cardiac death and ineligibility for machine perfusion, according to the criteria of the local organ-procurement organization. Thus, 910 donors (1820 kidneys) met the inclusion criteria. After the disenrollment of 21 donors (primarily because of withdrawal of research authorization) and the exclusion of 429 kidneys because of physician discard, lack of recovery, or use in research, 1349 kidneys obtained from 725 donors were transplanted: 359 kidneys from the hypothermia group, 511 from the machine-perfusion group, and 479 from the combination-therapy group (Fig. 1 and Table S4). (In the machine-perfusion group, one patient received two kidneys, so 511 kidneys were transplanted into 510 patients.) Two organ-procurement organizations performed machine perfusion in all kidney donors, whereas the remaining four organ-procurement organizations performed machine perfusion selectively.

At the first prespecified interim analysis after the enrollment of 600 donors, the hypothermia group met the prespecified criteria for inferiority as compared with both the machine-perfusion group and the combination-therapy group. The data and safety monitoring board recommended that the hypothermia group be dropped for inferiority after January 19, 2020, and that the randomization plan be changed accordingly. Subsequent donors were randomly assigned to receive machine perfusion of both kidneys with either normothermia or hypothermia (randomization plan 2 in Fig. S1). The design was revised to lower the maximum planned sample size to 1200 donors and to add a futility stopping rule for the remaining comparison between machine perfusion and combination therapy. At the second prespecified interim analysis after the enrollment of 800 donors, the data and safety monitoring board recommended that the trial be stopped for expected futility in showing the superiority of combination therapy over machine perfusion alone. Enrollment and randomization did not pause during the interim analyses.

Machine perfusion was not performed in 269 of 989 kidneys (27%) because of graft issues or logistic constraints caused by immediate long-distance air transportation needs.[3] Conversely, 41 of 359 kidneys (11%) in the hypothermia group underwent machine perfusion because of logistic constraints at the transplantation hospital or anticipated very long cold-ischemia times.

CHARACTERISTICS OF DONORS AND RECIPIENTS

Characteristics of the kidneys obtained from donors in the primary analysis population are summarized in Table 1. Donor characteristics (including the Kidney Donor Profile Index) were similar among the three treatment groups.

Recipient characteristics according to treatment group are summarized in Table 2. Recipients did not undergo randomization, because kidneys were assigned to them through the usual organ-assignment process. However, recipient characteristics that are known to affect kidney-graft survival were also well balanced among the three treatment groups. The mean (±SD) cold-ischemia

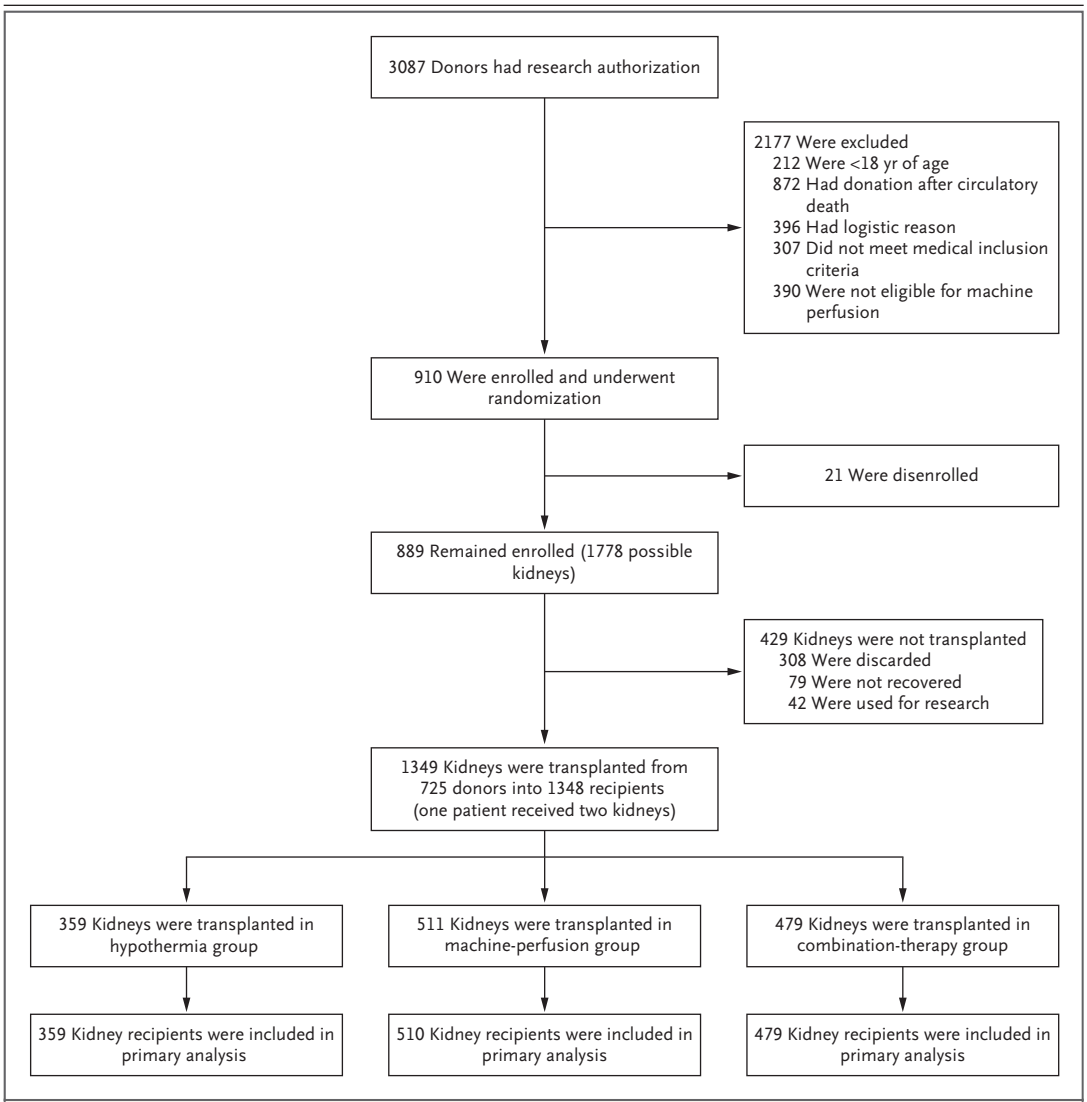

Figure 1. Assessment, Randomization, and Inclusion of Brain-Dead Donors.

Kidney donors were excluded after circulatory determination of death. Brain-dead donors were considered to be ineligible for logistic reasons if they were younger than 18 years of age, had a medical condition that precluded kidney donation, or had received a declaration of death for criteria other than neurologic. In the machine-perfusion group, one patient received two kidneys, so the number of kidneys in that category totals 511 rather than 510. All 1349 transplanted kidneys that were included in the primary analysis had known outcomes with respect to delayed graft function at 1 year.

time in the hypothermia group was 16.7±8.3 hours, as compared with 19.3±8.3 hours in the machine-perfusion group and 19.1±8.0 hours in the combination-therapy group.

PRIMARY OUTCOME

Delayed graft function occurred in 109 of 359 patients (30%) in the hypothermia group, in 99 of 510 patients (19%) in the machine-perfusion group, and in 103 of 479 patients (22%) in the combination-therapy group. In the primary efficacy analysis, the model-adjusted odds ratio was 2.21 (95% confidence interval [CI], 1.57 to 3.1) for hypothermia as compared with machine perfusion, 1.93 (95% CI, 1.39 to 2.69) for hypothermia as compared with combination therapy, and 1.14 (95% CI, 0.82 to 1.60) for combination therapy as compared with machine perfusion. In

Table 1. Characteristics of Kidney Donors in the Primary Analysis Population.*

Characteristic	All Donors (N=1348)	Hypothermia (N=359)	Machine Perfusion (N=510)	Combination Therapy (N=479)
Age — yr	42±14	41±14	42±13	42±14
Sex — no. (%)				
Female	508 (38)	137 (38)	191 (37)	180 (38)
Male	841 (62)	222 (62)	320 (63)	299 (62)
Height — cm	171±10	171±10	172±10	171±10
Weight — kg	86±24	85±23	89±25	85±23
Body-mass index†	29±8	29±7	30±8	29±7
Donation criteria — no. (%)‡				
Expanded	272 (20)	67 (19)	107 (21)	98 (20)
Standard	1077 (80)	292 (81)	404 (79)	381 (80)
Kidney Donor Profile Index§	46.40±28.98	44.25±28.95	47.95±28.74	46.36±29.22
Previous hypothermia treatment				
No	1121 (83)	290 (81)	445 (87)	386 (81)
Yes	228 (17)	69 (19)	66 (13)	93 (19)
Creatinine level — mg/dl				
At enrollment	1.35±0.84	1.32±0.8	1.34±0.86	1.37±0.84
Before transplantation	1.27±1.13	1.13±0.88	1.44±1.35	1.19±1.03
Estimated GFR — ml/min/1.73 m^2¶				
At enrollment	79±35	79±35	80±36	77±34
Before transplantation	91±40	96±39	84±39	94±40
Organ-procurement organization — no. (%)‖				
Number 28	730 (54)	194 (54)	276 (54)	260 (54)
Number 2	52 (4)	12 (3)	20 (4)	20 (4)
Number 29	13 (1)	2 (1)	8 (2)	3 (1)
Number 34	241 (18)	66 (18)	84 (16)	91 (19)
Number 37	277 (21)	79 (22)	104 (20)	94 (20)
Number 40	36 (3)	6 (2)	19 (4)	11 (2)

* Plus–minus values are means ±SD. Included in the primary analysis were all organ donors who had contributed at least one kidney with a known outcome for delayed graft function. In the machine-perfusion group, one patient received two kidneys, so the numbers of kidneys in each category total 511 rather than 510.

† The body-mass index is the weight in kilograms divided by the square of the height in meters.

‡ Standard criteria were a declaration of brain death according to hospital criteria for neurologic determination of death and an age of 18 to 50 years or an age of 51 to 59 years with no more than one of the following coexisting illnesses: chronic hypertension, death resulting from a cerebral vascular accident, or a serum creatinine level of more than 1.5 mg per deciliter. Expanded criteria were a declaration of brain death according to hospital criteria for neurologic determination of death and an age of more than 59 years or an age of 51 to 59 years with at least two of the previously listed coexisting illnesses.

§ The Kidney Donor Profile Index is a cumulative percentage scale that represents an overall estimate of the risk of graft failure for an individual kidney. Scores range from 0 to 100%, with higher values indicating greater risk.

¶ The estimated glomerular filtration rate (GFR) was determined with the use of the Modification of Diet in Renal Disease formula.

‖ The names of the organ-procurement organizations are provided on page 3 in the Supplementary Appendix.

protecting kidney-graft recipients from delayed graft function, hypothermia was inferior to machine perfusion, and combination therapy was not superior to machine perfusion. The effects of covariates are listed in Table S5.

Adjusted risk ratios for delayed graft function were 1.72 (95% CI, 1.35 to 2.17) for hypothermia as compared with machine perfusion, 1.57 (95% CI, 1.26 to 1.96) for hypothermia as compared with combination therapy, and 1.09 (95% CI,

Table 2. Primary Outcome and Characteristics of Kidney Recipients at Baseline.*

Variable	All Recipients (N = 1348)	Hypothermia (N = 359)	Machine Perfusion (N = 510)	Combination Therapy (N = 479)
Primary outcome				
Delayed graft function				
No	1038 (77)	250 (70)	412 (81)	376 (78)
Yes	311 (23)	109 (30)	99 (19)	103 (22)
Characteristics at baseline				
Age — yr	52±15	51±16	52±14	51±15
Sex — no. (%)				
Female	529 (39)	143 (40)	192 (38)	194 (41)
Male	820 (61)	216 (60)	319 (63)	285 (59)
Height — cm	168±14	168±16	168±13	168±14
Weight — kg	80±21	81±23	80±20	80±21
Donor-to-recipient weight ratio	1.2±0.6	1.2±0.7	1.2±0.5	1.2±0.5
Body-mass index	28±10	29±16	28±6	28±9
Kidney cold-ischemia time	18.5±8.4	16.7±8.3	19.3±8.3	19.1±8.0
Hepatitis C virus serostatus — no. (%)				
Positive	60 (4)	21 (6)	25 (5)	14 (3)
Negative	1277 (95)	335 (93)	482 (95)	460 (96)
Unknown or not measured	12 (<1)	3 (<1)	4 (<1)	4 (<1)
Human leukocyte antigen mismatch — no. per recipient	4.2±1.4	4.2±1.4	4.2±1.4	4.1±1.5
Panel reactive antibody†				
Mean — %	23.4±36.5	21.9±35.6	22.3±35.5	25.7±38.1
>80%	216 (16)	55 (15)	75 (15)	86 (18)
Placed within donor service area — no. (%)				
Yes	999 (74)	280 (78)	365 (72)	354 (74)
No	350 (26)	79 (22)	146 (29)	125 (26)
Duration of renal-replacement therapy before transplantation — days	1720±1259	1813±1268	1692±1353	1680±1146
Previous renal transplantation — no. (%)				
No	1208 (90)	333 (93)	456 (89)	419 (87)
Yes	141 (10)	26 (7)	55 (11)	60 (13)

* Plus–minus values are means ±SD. In the machine-perfusion group, one patient received two kidneys, so the numbers of kidneys in each category total 511 rather than 510.
† The score for panel reactive antibody is expressed as a percentage from 0 to 100. It represents the proportion of the population to which the person being tested will react through preexisting antibodies against human cell-surface antigens.

0.85 to 1.40) for combination therapy as compared with machine perfusion (Table 3).

SECONDARY OUTCOMES

The frequency of kidney graft survival was similar among the three groups at 1 year. The Kaplan–Meier estimated 1-year kidney survival results are provided in Figure S2 and Table S6; the results of Poisson generalized-estimating-equation regression regarding 1-year kidney graft failure are provided in Table 3. Among all 1348 kidney recipients, 45 recipients died within 1 year of follow-up; of these recipients, 8 (2%) were in the hypothermia group, 19 (4%) in the machine-

perfusion group, and 18 (4%) in the combination-therapy group.

The number of organs that were transplanted according to donor and treatment group are provided in Table S7; 1-year graft failure for transplanted liver, heart, lung, and pancreas are summarized in Table S8. A total of 10 adverse events were reported among the donors, including cardiovascular instability in 9 donors and organ loss in 1 donor caused by machine-perfusion malfunction (Table S9). The representativeness of donors and recipients are described in Tables S10 and S11, respectively.

Table 3. Primary and Key Secondary Kidney Graft Outcomes.*

Variable	Treatment Effect (95% CI)†	
	Unadjusted	Adjusted
Delayed graft function‡		
Hypothermia vs. machine perfusion	1.56 (1.23–1.98)	1.72 (1.35–2.17)
Hypothermia vs. combination therapy	1.41 (1.12–1.78)	1.57 (1.26–1.96)
Combination therapy vs. machine perfusion	1.11 (0.87–1.42)	1.09 (0.85–1.40)
Graft failure at 1 year§		
Hypothermia vs. machine perfusion	0.74 (0.33–1.66)	NA
Hypothermia vs. combination therapy	0.91 (0.40–2.06)	NA
Combination therapy vs. machine perfusion	0.82 (0.40–1.67)	NA

* NA denotes not applicable.
† The treatment effect was calculated as a risk ratio for delayed graft function and as a hazard ratio for graft failure at 1 year. The statistical analysis plan stipulated the calculation of odds ratios, which are reported in the Primary Outcome section.
‡ The results for delayed graft function (the primary outcome) were calculated from generalized-estimating-equation modeling of Poisson regression with log-link and exchangeable correlation structure after adjustment for the same prespecified covariates as were used in the primary analysis. A relative risk of less than 1 indicates a lower risk of delayed graft function, and relative risk of 1 or more indicates a higher risk of delayed graft function.
§ Graft failure at 1 year (a secondary outcome) was calculated with the use of a Cox regression model after adjustment for the randomized treatment assignment. A hazard ratio of less than 1 indicates a lower risk of graft failure. Robust standard errors were used to account for correlation between kidneys from a single donor. Additional covariate adjustment could not be performed because of a small number or no events within subgroups of covariates. In tests for secondary outcomes, there was no provision for multiple comparisons, so results are reported as point estimates and 95% confidence intervals. The widths of the confidence intervals have not been adjusted for multiplicity, so the intervals should not be used to infer definitive associations.

DISCUSSION

We designed this prospective, randomized trial involving brain-dead organ donors who were eligible for hypothermic machine perfusion to determine whether hypothermia (34 to 35°C) in the donor would be noninferior to machine perfusion to reduce the risk of delayed graft function in the transplant recipients. The trial was terminated early because an interim analysis established the inferiority of hypothermia alone as compared with either machine perfusion alone or a combination of the two strategies. An interim analysis also showed a lack of a benefit for the combination strategy over machine perfusion alone. The observed incidence of delayed graft function was reduced by 11 percentage points in the machine-perfusion group as compared with the hypothermia group (19% versus 30%). The frequency of 1-year graft survival among the kidney recipients was similar in the three groups.

Machine perfusion of kidneys obtained from brain-dead donors is currently performed in approximately 32 to 38% of all kidneys considered for transplantation in the United States. Although several meta-analyses have reviewed the results of trials examining machine perfusion of the kidney,[8,9] data from large, prospective trials are lacking. One large, randomized trial in Europe showed a benefit for machine perfusion as compared with static cold preservation and with no intervention in the donor.[2] Our findings provide additional evidence that machine perfusion protects against delayed graft function as compared with static cold storage, even when the donor was undergoing therapeutic hypothermia. Of note, among the donors who were assigned to undergo machine perfusion, the procedure was not performed in 27% because of graft issues or logistic constraints. This percentage is substantially higher than a previously reported percentage of donors who underwent successful machine perfusion.[2] The reasons for the observed difference may include varying practice and geographic requirements for kidney assignments and trial-specific design differences. In the European trial, 1-year graft survival was better with machine perfusion than with static cold storage. This finding also contrasts with our trial results, which showed no benefit for machine perfusion on 1-year allograft survival, although we did not use static cold storage as a

control strategy. Finally, our findings with respect to delayed graft function in the hypothermia group were similar to the incidence in the hypothermia group in our previous trial, results that were numerically lower than those in the control group in that trial.[1] As we found in our previous trial,[10] the overall failure of nonkidney organ transplants was less than 5% in all three treatment groups.

A limitation of our trial was the open design in which all health care providers were aware of the group assignments. However, the investigators were not involved in the outcome-assessment process.

We found that machine perfusion of kidneys obtained from brain-dead donors provided better protection against delayed graft function than targeted mild hypothermia alone. The combination of hypothermia and machine perfusion was not superior to machine perfusion alone in decreasing the incidence of delayed graft function.

The data reported here have been supplied by the United Network for Organ Sharing as the contractor for the Organ Procurement and Transplantation Network (OPTN). The OPTN data system includes data on all donors, wait-listed candidates, and transplant recipients in the United States, as submitted by OPTN members. The Health Resources and Services Administration of the Department of Health and Human Services provides oversight of the activities of the OPTN contractor. The interpretation and reporting of these data are the responsibility of the authors and in no way reflect the official views of the OPTN or the U.S. government.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

A data sharing statement provided by the authors is available with the full text of this article at NEJM.org.

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