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Discussion

DR. RONALD W. BUSUTTIL (Los Angeles, California): Dr. Broelsch and his colleagues have focused their attention on the dire problem of the existing shortage of pediatric donors for critically ill children with end-stage liver disease. In this presentation they have reported their experience with reduced size organ transplantation in a group of 14 children urgently in need of liver replacement. These pediatric patients had the usual indications for urgent liver grafting, including retransplantation, fulminant hepatic failure, and rapidly aggressive chronic liver disease. The technique used has been previously described and is based on the anatomic removal of hepatic segments to allow a suitable fit into a small recipient. The use of the left lobe is most appealing, in that it requires minimal tailoring of the vena cava and avoids the potential problem of bile duct necrosis that can occur when a left lateral segment is used alone.

Using a reduced liver graft, six of ten patients who underwent primary transplantation survived. However, only one of four patients who were retransplanted with a reduced graft survived. This is discouraging, because it seems that retransplantation would be the Number One indication for a reduced size organ graft.

What is of further concern is that the reduced organ is fraught with a 70% incidence of graft complications. These range from global graft ischemic damage to both hepatic artery and portal vein thrombosis. To put this into perspective, I have looked at our own experience with pediatric liver transplantation at UCLA, and specifically, at that subgroup of patients who we would consider to be potential candidates for reduced size livers—namely, those pediatric patients who were in urgent need of retransplantation.

(Slide) Two hundred fifty-nine liver transplants were performed at UCLA between February 1, 1984 and April 15, 1988. Of these 259 cases, 109 pediatric liver transplants were performed on 91 children. These children ranged in age from 5 months to 15 years, with a mean of 5 years. Our overall 4-year actuarial survival rate of these 91 patients is currently 80%. Eighteen of these children required retransplantation and make up the group shown on the bottom curve. Indications for retransplantation included hepatic artery thrombosis (seven patients), primary nonfunction (four patients), and liver rejection (seven patients). For none of the patients who required retransplantation were we unable to find a donor. We mismatched blood groups in eleven cases and generally accepted even the so-called "bad donor."

What is clear is that these children did not do as well as those with primary grafts. However, their rate of survival is still significant, underscoring the benefits of an aggressive policy at retransplantation using only whole organs. Four-year actuarial survival of this group of 18 patients who underwent retransplantation is 61%. The reduced organ size graft technique is a novel one, and I commend Dr. Broelsch on his pioneering efforts. However, I would caution against its widespread acceptance until more experience is accumulated to properly define its role in pediatric liver transplantation.

I would like to conclude by asking three questions.

If one looks at the donor age and weight, which were used for reduced size organs, eight organs were of pediatric size, which we would prefer to use for a recipient of that size. Thus, isn't this technique potentially reducing the pool of grafts that might be more appropriately suited for those pediatric recipients who would have a more favorable prognosis?

There seems to be a higher incidence of infection and intracranial hemorrhage in these patients than one would anticipate with those having whole organ grafts. Dr. Broelsch, do you believe that this is due to greater graft ischemia or to the poor quality of the host in whom you are implanting the organ?

If one takes this technique one step further, do you feel that it is applicable to living related partial hepatic grafts?

DR. ROBERT J. CORRY (Iowa City, Iowa): I would like to compliment Dr. Broelsch and the other authors on this outstanding presentation, and I commend them on their application of a partial donor liver graft in overcoming the size disproportion of some children who, because of the limited number of pediatric donors, might not otherwise receive a liver graft.

Several years ago, Dr. Ron Malt of the Massachusetts General Hospital and I used partial liver grafts for heterotopic auxiliary transplantation in dogs, primates, and in one human. We believed that this procedure could be used as a bridge for those patients who might be able to recover their own liver function, and perhaps also be used as a permanent graft in high-risk patients.

As you are aware, at that time (20 years ago), the success rate of this technique as well as that of even the orthotopic technique was not good, and the heterotopic liver transplant procedure was abandoned in humans. However, as you know, auxiliary grafting has recently been applied in a few of the European programs with some long-term success, particularly in reoperative patients and other high-risk patients.

So my question, Chris, is whether or not you plan to extend this unique technique of transplanting a portion of the donor liver as either a bridge for patients who might recover their own liver function or possibly even as a permanent graft in high-risk patients.

DR. CHRISTOPH E. BROELSCH (Closing discussion): Thank you, Dr. Busuttil and Dr. Corry for your remarks. I believe that Dr. Busuttil pointed in the right direction regarding the application of this procedure; at the present time, urgent retransplantation is where the scarcity of donor organs in children is preeminent.

In most instances, the success of retransplantation relies on the immediate availability of organs. I haven't presented our data yet on the retransplanted children with full-size organs. When you get a full-size organ within 24 hours after the decision for retransplant has been made, the results certainly will be better.

In the past, we would wait 24 hours or even 48 hours to get a full-size graft first, and when this didn't succeed, we would increase the weight range of the donor to get any piece of liver in order to attempt the

salvage. I believe that, by using the reduced size earlier than we did, we may reduce the relatively high lethality in the retransplant population.

Furthermore, you mentioned that we are depriving the pool of potential pediatric donors by using reduced size grafts. In fact, we performed this procedure in two babies in whom we initially attempted to perform a full-size graft procedure. Before operation was performed, it turned out that the grafts were too large in size, and they had to be reduced in size before grafting. But, whatever the size of the graft, by using the technology available and being flexible in reducing the size of the graft, one can make a perfect fit into the potential recipient.

We performed the procedure in six other children who were between 2 and 13 years of age. As you know, the overall pool of donors in that relatively larger group of children is larger than that of babies because of the mechanisms of death; school children run into cars and are pronounced brain dead, whereas this does not occur with babies. In general, the pool of donors in the adolescent age group is larger than that of infants, whereas there is less demand for such donors because of the incidences of liver diseases. The donor pool of older children is where we probably will focus the application of this procedure.

The graft complications have been a problem to us, especially ischemia. As I have said, we have experienced 2.5 hours longer ischemia time in those operations using partial grafts as compared with those using the full-size grafts. Whether this is attributable to initial malfunction or whether the marginal circulation or the advanced disease of the recipient is the cause, I don't have clue.

Hemorrhaging of the brain occurred in three of our cases. I believe this was due to the fact that the graft was partially functioning. These children are in renal failure, they are overloaded with fluid, and they have liver failure. These conditions may contribute to brain edema, and that may just set the situation for receiving an intracranial bleed. Surprisingly to us, we have never observed a bleeding from the raw liver surface and no infection from the cut surface, although we are not using glue or adhesives to seal off the cut liver surface.

Hepatic arterial thrombosis was seen in only one case, and that was a surprise because in using this procedure, the group in Belgium, together with other groups in Hannover, Paris, and Innsbruck, have reported a few incidents of hepatic arterial thrombosis. In all 14 cases that we dealt with, we observed only one incidence, which is likewise low.

In one patient, we observed a portal vein thrombosis. We tried to remove it, and the patient subsequently required a splenorenal shunt and is now doing fine 18 months after surgery.

Speculatively, turning toward the scope of where this technology could be applied in the future, striking idea one must consider is living related donors for grafts. I strongly believe that we will be using this technique one day because many babies younger than two years of age do not otherwise have a large donor pool. We hope to show in the laboratory that the living related model works in dogs and provides long-term survival.

We may then, with a profound ethical background, even embark on such a trial in humans.

Conceptually, the situation is different than in segmental pancreatic grafts or in living related renal transplants because the liver regenerates completely.

Dr. Corry, regarding your question about the heterotopic concepts, I believe we are all aware of the work of yourself, Dr. Malt, Dr. Price, and others, such as Dr. Wexler, who did exciting work on autologous lobe liver transplantation. I believe you have shown us the technique for performing this in dogs, as well as how to pursue this concept further.

However, I learned from the rat model, when I worked with Dr. Orloff in the laboratory, that there is a problem with hepatic venous outflow. If you put a transplant in the heterotopic position somewhere in the abdominal cavity, it is going to atrophy and will not survive very long. You have to put it into a favorable outflow position that is close to the diaphragm and close to the liver. And, indeed, the only long-term survivor with a heterotopic auxiliary transplant lived 4 years. The small pediatric graft was placed into a heterotopic position right underneath the diaphragm so that it had a favorable outflow condition.