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Discussion

DR. HENRI BISMUTH (Villejuif, France): I would like first to congratulate Dr. Rogiers and Dr. Broelsch for their innovative procedure of splitting the liver *in situ* for grafting. Indeed, they transpose to the cadaveric donor the technique used for harvesting the left lobe in the living donor, and they show how successful this is. There are three types of liver grafts beside the classical whole liver graft: 1) the reduced-size graft, which makes the graft smaller—it changes the recipient from being an adult to a child but it brings no benefit to the pool of available grafts; 2) The graft from a living donor; and 3) the split-liver graft. Both the latter techniques increase the number of livers available for patients in the waiting list.

I would like to focus on the split liver. In our center, we have developed since January 1995 a policy of systematically considering for splitting all grafts offered to us which appear suitable for this technique. During the last year, we performed 27 split-liver procedures out of 90 transplantations, representing an increase in available grafts of 30%. One-year patient survival rate is 80%, similar to patients transplanted with a whole graft in our center, showing that the increase in the number of grafts was not obtained at an extra cost by the recipients. The authors say that the reduced-size graft has no more indication; even thinking about the great enthusiasm among liver transplant surgeons when this technique was introduced 10 years ago, I totally agree with them.

Dr. Rogiers says that the *in situ* liver splitting technique gives similar results in children as the partial graft coming from a living related donor. I would then ask whether there is any justification for using living donors instead of the split-liver technique in countries where cadaveric donors are available, such as North America and Europe. For even if the risk for the living donor is small, it exists, and by definition, this risk is zero in a cadaveric donor. This is an important ethical point; even if we consider that we may split only 15% of the grafts, these split livers will cover almost all the needs for pediatric liver transplantation.

I thank Dr. Broelsch for giving me the privilege to read his excellent paper before the meeting and to comment on it in front of you.

DR. JEAN EMOND (San Francisco, California): The concept of splitting livers was born in Henri Bismuth's school in Paris and in the Pichlmyr School in Germany nearly 10 years ago. Our initial efforts in Chicago were plagued by technical failures and errors in patient selection. In the present report, we learn of the optimal approach to this appealing therapy with nearly perfect results that could theoretically double the donor supply.

The clear advantage of splitting *in situ* is the reduction of the cold time and the back table preparation, which takes up to 4 hours to make two good grafts, and greater accuracy and safety in dissection. The down side, which was not addressed, is the prolongation of the donor operation, inconveniencing a number of teams, and the performance of a complex dissection under difficult conditions in the whole spectrum of hospitals with operating room teams, which occasionally are indifferent or even hostile to the concept of transplantation.

The relationship between split livers and living donors has been symbiotic. In 1988, the success of a few early cases of split livers gave us confidence that living donors were feasible. Recently, the many lessons of living donors have permitted us to improve split-liver transplants. In San Francisco, all four cases of split livers have resulted in good results without using *in situ* dissection.

So my first question is, what is the added benefit of the *in situ* dissection? Is it possible that the recent improvements reflect the learning curve as much as the change in technique?

The only failure clearly attributed to the graft in your series was an attempt to treat two adults. Are splits going to be limited to adult and child pairs? If this is the case, only 10% of orthotopic liver transplantation candidates are children, so perhaps the benefit of splits will be limited.

In the classical reduced liver, the right lobe is discarded. Are you prepared now to relegate that operation to the museum and offer all right lobes to adults?

Finally, as experience is gained, would you be prepared to mandate splitting of all livers?

DR. CHARLES MILLER (New York, New York): I would just like to briefly capsulize our split data from New York City.

We have done split liver transplants in 11 patients. The first ten were done from five donors using an *ex situ* back table technique, in which we discarded segment 4, as Dr. Broelsch had originally described. The final case was a long distance *in situ* split, where we went to Oklahoma, split the liver, and brought back the right lobe. It worked beautifully, just as Dr. Broelsch described. That patient went home in 10 days.

The most striking difference between our group of patients and Dr. Broelsch's is the amount of very highly urgent patients that we were forced to transplant with this technique. We transplanted 9 of our 11 patients as status 1 or status 2, while I think the majority of his patients were highly elective cases. We did not want to get into that, but we were forced by the clinical reality to move in that direction.

Unfortunately—and I believe because of this—there were four deaths in our series, all in the *ex vivo* split group. Two deaths occurred from primary nonfunction of both grafts from a single liver. It was a damaged liver, we should never have used it, and it killed both recipients within 24 hours of the implantation. It almost killed the transplant team. There was one technical error that caused portal vein thrombosis and graft loss. One other adult, who had waited for a week in the intensive

care unit in a coma, almost anhepatic, was a very poor candidate and died in 2 weeks from sepsis.

The point is that it is difficult to attribute any of these failures to the donor or back table operation technique, but rather poor donor or recipient choices in three cases and one unfortunate technical complication in the fourth. On the other hand, we did also have two bile leaks that maybe could have been avoided by leaving segment 4 intact, as the *in situ* split technique demands.

Finally, based on our experience with the *ex vivo* and the one *in situ,* we feel that the *in situ* split is a very good alternative. It really does allow easy logistics of sending livers to two different centers. There is much easier hemostasis on a very small cut area. We feel that it is probably a technique for the future, but we have certain concerns, and I have certain comments.

Dr. Broelsch, you have clearly shown that it is safe in approximately 90% of the cases to leave segment 4 behind. Can you identify any anatomic or any other characteristics that can predict when segment 4 will be nonviable? Can you explain in any anatomic or physiologic terms why it should stay alive?

Is perioperative hemodynamic stability of the recipient an important issue? Does the benefit of your new technique emanate from the fundamental simplicity of a single small plane of division at the umbilical fissure or from the fact that it is done *in situ*? In other words, could not equally good results, as actually have been reported by some other authors, have been attained by simple technical division on the back bench? Do you have any data that show that there was significant warming on the back table during your other splits?

Is it possible that your excellent results are actually attributable mostly to donor and recipient selection, as evidenced by the high proportion of status 4-type elective cases as well as using only the most stable donors to employ this *in situ* split? Do you have comparable demographics of your two groups with respect to donors and recipients?

Are there special guidelines for *in situ* donors, such as age restrictions or the use or lack of need for suppressor support? Interestingly, the single mortality in your series was in an adult—and this speaks to Dr. Jean Emond's point—who received a left lateral segment graft that was probably of insufficient size to get through an ischemic injury followed by a rejection.

With regard to the *in situ* technique representing the means of the ultimate expansion of the donor pool, it must be remembered that only 7% to 10% of children can benefit from this, and that is the real limit, unless we open this up to formal left–right lobe splits. Do you think your *in situ* technique will be appropriate and beneficial in this formal left–right lobe by partition? Or will the venous drainage of the right graft still be problematic?

DR. JOHN S. NAJARIAN (Minneapolis, Minnesota): I, too, would like to congratulate the authors. Chris Broelsch has done us a great service by demonstrating the feasibility of living related transplants of liver segments from adults into children. I think this is an extremely important observation, considering the limited supply of pediatric liver donors.

The authors are now applying similar techniques to preparing split donor livers for transplantation. I agree this may be an important way of expanding the donor liver pool. The limited number of donor livers is certainly a major concern for all of us in transplantation. The donor shortage becomes even more evident as the number of recipients continues to grow, while the number of donors remains constant.

We have had very little experience using split donor livers. We have, however, transplanted a fair number of reduced donor liver segments into children. I think the authors' technique of splitting the donor liver *in situ* is good. Yet the delay in procuring other potential organs from the donor may become the real Achilles heel of this operation.

What I would like to report on today is our experience with living donor pancreas transplantation. We have performed 89 pancreas transplants from living related donors using the tail of the pancreas. We now know that the tail of the pancreas is quite adequate for a successful transplant and allows diabetic recipients to become insulin independent.

As a result of our experience, we once performed a split pancreas transplant from a single donor using the tail for one recipient and the head for a second recipient. Both recipients had 100% preformed antibodies and a negative crossmatch to the donor. So we were able to use both the head and the tail. We were pleased that both transplants were successful. The head functioned for 8 years. The tail functioned for about 9 months but was eventually rejected.

Our experience demonstrates that split donor organ transplants may also expand the donor pool for pancreas recipients as well. Doing so is not yet urgent. Because few transplant units currently perform pancreas transplants, the supply of donor pancreases is adequate for now. But this split donor technique can be used when the supply of donor pancreases also becomes limited or under special circumstances, as I described.

I just have one question to ask. I noticed that when left lateral liver segments were transplanted, two of these segments were not successful. I wonder if their size was inadequate, or was there some other complication to account for these losses?

DR. JEREMIAH G. TURCOTTE (Ann Arbor, Michigan): I want to thank Dr. Broelsch for asking me to discuss this important paper and providing the manuscript for me to read. He has asked me to emphasize the logistics of liver transplantation and the donor shortage.

Dr. Broelsch, of course, pioneered volunteer liver donor transplantation while he was at the University of Chicago. His paper today in which he describes *in situ* split cadaveric liver transplantation has the potential of significantly relieving the very acute shortage of donor livers that exists in the United States and most other countries. More than ten times as many people die of liver disease in the United States as we are able to transplant. Eight percent of patients on the waiting list for receiving liver transplants die, and this is probably an underestimate. The donor situation is analogous to military triage, in which the number of injured patients overwhelms available resources, and what resources are available are necessarily triaged to those who are both in need of intervention and also have a good chance of surviving.

For split-liver transplantation to be applied widely, organized plans will need to be in place to achieve cooperation between transplant centers and donor hospitals. At times, one donor liver segment from a split liver will have to be transplanted

at one hospital and the other segment of the transplant at a second hospital. At our hospital, we transplant all the major organs. At times, four or more operating rooms are needed almost simultaneously on a nonscheduled basis for a heart, two lungs, pancreas, liver, and a kidney transplant. Few hospitals have the capability of adding a second liver transplant or even doing two liver transplants simultaneously.

My questions for Dr. Broelsch are: How do you organize the logistics in your own transplant center when you have two grafts available at the same time? Are you always able to perform both transplants in your own center? Do you take into account any allocation criteria, such as waiting time, when considering what center or patient should have the second half of the split graft?

DR. CHRISTOPH E. BROELSCH (Closing Discussion): Dr. Bismuth, I thank you particularly for your final question: Is there any more justification now for living related organ transplantation with the spectrum of split livers being performed *in situ* or *ex situ,* enlarging the donor pool?

First of all, we need to take advantage of any method of enlarging the donor pool by one way or the other, including living related liver transplantation. After many controversial discussions it was finally possible to convince the transplantation community about this procedure. Now I should definitely state, that this is still the best procedure a child can have today.

The other alternative we are offering, split liver and especially reduced liver, are the disputable ones. You and Dr. Emond mentioned that reduced-size liver transplantation may become obsolete. I believe, too, that it will have to become obsolete or should only be performed in cases of traumatized livers, in which one of the liver lobes is damaged and the other side can only be used for transplantation, or, in cases when the donor liver is too small to allow safe splitting. In the future any other approach, *i.e.,* taking a whole liver and benching it down for one small recipient only, will require justification. So I think we have a consensus regarding your question.

As to Dr. Emond's question, will there be a place for splitting between two adult recipients? Right now there is a limit to children–adult or adult–adult pairs. I propose that in the future, we should organize a system within organ procurement agencies that takes into account size matches, liver anatomy, and liver volume. Perhaps some centers can start with agreements establishing a network for sharing split organs, based upon requirements of specific recipients (children, small adults, candidates for auxiliary transplantation, etc.). This is also an answer to one of Dr. Turcotte's questions. I think the rules for organ allocation and the logistics require adaptation to these innovations in order to allow their optimal use.

The quality of the other organs procured, asked about by Dr. Najarian, has caught our special attention. All procedures were performed in multiorgan donors. All 14 kidneys, 2 pancreases, and 5 hearts procured had excellent initial function. So it is possible to accommodate all other teams if they show some good will. I believe if some other institutions confirm our good results, it shall convince the transplantation community that this can be an additional way to optimize the use of our resources. Dr. Turcotte indicated that 4800 liver transplants are being done annually. If we could only utilize 20% more, that would be a considerable number, providing more chances of being treated for many patients.

Dr. Miller, I really appreciate your comments, particularly your coming especially to discuss our paper. The question about segment 4 is, and has always been, a crucial one. There are really no reliable predictors of its salvageability, either by angiogram or by Doppler ultrasound. Frequently, there are one or more small arterial branches coming off the right hepatic artery which can be preserved. You only recognize those as you are dissecting free the right side of the round ligament and transecting the portal branches to segment 4. By doing this as a bench procedure, one easily misses these, with the consequence that they are being destroyed, resulting in ischemia of the lobe.

Regarding reoperations on the bile duct, many previous problems may have been caused by dissection of the biliary confluence, causing devascularization and ischemia. Since we have started to avoid the area of the bifurcation by severing the bile duct only at its entrance into the left lateral lobe, the problems with bile duct complications have disappeared.

As to the matter of patient selection, we have not performed any specific patient selection, except to avoid performing two high-risk transplantations at the same time, in order to avoid overstressing our hospital's resources in case of complications. Three of the 14 recipients were on high urgency code, another two were United Network for Organ Sharing (UNOS) status 2, and the others were rather elective patients.

From your experience with *in situ* split procedures, you describe exactly what everybody realizes when performing this procedure. It simply works, with excellent initial graft function! I believe this is because one ends up with two perfectly viable grafts. After removal of the left lateral lobe the pediatric team, if the others agree, can leave the donor hospital, leaving the adult team to remove the residual right liver whenever necessary. This significantly decreases the ischemic times for both sides.

The last question focuses around the formal right and left lobe splitting in the future for adult recipients. It turned out that, with living related and *in situ* split liver, the whole pediatric population can be supplied now. Actually, there should not be a child dying on the waiting list anywhere because of all the possibilities we have now. But what about the adults? The slender 45-kg patient with a small Asian-type stature should do perfectly with a 450 mL or 500 mL left lateral lobe, and somebody else may benefit from the extended right lobe. So I think it is a matter of first matching those pairs between centers that are willing to cooperate. In a second step, large volume livers from ideal donors should be used to serve adult recipients.

As to the cause of graft loss, Dr. Najarian, one graft was lost because we had a 480-mL graft in a 54-kg patient which failed and required retransplantation after an episode of rejection. One patient was lost from complications after retransplantation for progressive inferior vena cava thrombosis, obstructing the venous outflow. The thrombosis was probably caused by protein S deficiency, transmitted from the donor through liver transplantation. The recipient of the other split half also has the coagulation disorder but is fortunately doing fine.