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INTERVIEW
of Dr Jiří Froněk
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Pioneering Czech work, with genuine value to society

Dr Jiří Froněk, head of the surgery transplantation clinic, and his team of doctors at IKEM, split a liver and transplanted it into two adult recipients. This operation, on a husband and wife who had been poisoned by a death cap mushroom, was the first of its kind anywhere in the world.



When did doctors first begin to consider the idea of splitting a liver?

The idea first appeared in medical literature in the 1960s. It was first done in the 1980s, and in the mid-1990s the programme began to expand, mainly because child recipients of livers on the waiting list have a far higher morbidity and mortality rate and sadly often die because they wait in vain for a liver of suitable dimensions from a child donor.

The classic split, whereby the second and third segments of the left lobe are given to the child and the rest to an adult, is a commonly used technique nowadays. This resolves the shortage of livers for child recipients and enables adults on the transplant waiting list to be treated. When high-quality livers are offered for transplant, it would be a great pity to proceed by means of reduction. This procedure means a smaller liver for one recipient, often a child; of course the remainder could not be used for another transplant. The split technique has formed part of our programme since January this year. For every liver that meets the criteria for splitting we have always considered a split for an adult and a child, but not for two adults.

Does the future lie in the splitting of donor livers between two adults?

This method has appeared in specialist literature since 2000. In a number of countries, and in particular in the United States, recipients in a very poor state of health find themselves on the waiting list. Many wait a long time, often in vain, for a liver. It is therefore, in principle, desirable to treat two recipients with one liver. This has its downsides, however: for example, a higher incidence of certain complications, so one prerequisite is that the liver must be of excellent quality. Another problem is small-for-size syndrome (SFSS). At the point where we split the liver, its volume must be sufficient for the recipients' liver functions. The recipients' weight, and the expected required volume of the transplanted part of the liver in both recipients, must therefore be measured very carefully.

Livers have a large incidence of anatomical anomalies in the arteries and veins. When splitting one, a thorough analysis must be made of the risk of vein anomalies. Where the liver graft does not enable sufficient vein outflow, it will not begin to function properly or will do so only for a limited amount of time. The incidence of vascular anomalies in donors is very difficult to detect, and as such difficult to treat.

Does the technique used in liver sampling play a part?

Yes. In this case, we opted for a split *in situ*. The advantage of sampling in the donor's body is shorter cold ischemia time, which increases the hope that the transplant will be successful. However, it is technically difficult to perform and may be affected by blood loss, which is liable to compromise not only the liver itself but also other organs suitable for transplantation. Younger donors are often capable of donating more than one organ, which is something we need to take into account when we perform this intervention.

The second *ex-vivo* technique spares other organs but is not beneficial in terms of accurate recognition of the anatomy of the liver and treatment of the structure when it is split. In such cases there is a higher chance of post-transplant haemorrhage and of bile outflow from the area after splitting. The choice of technique does not always rest with the surgeon. In many countries this is a logistical problem. For example, in the UK or USA the liver or parts thereof travel long distances and it is not realistically possible to carry out both sampling and transplants at a single centre. In this regard, we are at a relative advantage because when we decide to split a liver we try to carry out the sampling at the IKEM. There was just one case when I went to Motol Hospital to split a liver because of the quality of the lungs.

How exactly does the splitting of a liver for two adults take place?

It is a technically different operation from the splitting of organs between a child and an adult; the liver must be split virtually symmetrically so that there is sufficient liver tissue for both recipients. Furthermore, there is no consensus, either in literature or in any techniques described by individuals, on where, for example, to keep the central hepatic vein; on the side of which graft to keep the inferior vena cava; or on the side of which part of the graft, after the split, to keep the main trunk of the bile duct or the arteries. The procedure is not a uniform one, for one thing because every liver has unique vascular anomalies and also because the organs vary between different races. As for the central hepatic vein, it can theoretically be left as part of both the left and right grafts, or split into two and kept on both sides, with a plastic aid, to help with vein replacement. Much depends, though, on the anatomical proportions of the liver itself.

Have your patients suffered any complications in this regard?

Both the graft and the recipient(s) can suffer complications. In the case of the graft, the key factor is the actual quality of the split and the amount of tissue in both parts of the liver. The size of the donor's liver was at the very limit of the requirements for both of our patients. During the procedure, vascular anomalies occurred, in particular in the venous part, i.e. discharge from the liver graft. It was only when the liver was split, rather than during pre-operative examinations, that we identified aberrations. On the other hand, I figured that it was worth attempting; I could not imagine how I would decide which of them to operate on when both were in such a poor state of health and, without a transplant, would soon have died. Both patients were at such an advanced stage of liver failure that they had perhaps one hour to live.

The case was complicated by the fact that one of the recipients had a different blood group from the donor. It was therefore necessary to spend a number of hours removing the antibodies to the blood group of the liver graft. We did not perform the treatment by plasmapheresis, which we had used a number of times before in cases of acute liver failure in AB0-incompatible recipients. We therefore opted to perform what is known as non-selective immunoadsorption. For some cases of this kind, this method is perhaps more suitable because it enables us to protect certain components which plasma

exchange does not enable us to do. It was a success thanks to the colleagues who performed this part of the intervention and managed to reduce (and keep at a low level) the antibody titres. We repeated the adsorption several days after the transplant. The above method makes it possible to repeat adsorption using the same capsules for a period of one year if the patient's state of health calls for this. As things stand, however, it is not necessary to continue with this treatment. Both patients have undergone successful transplants and will be allowed home in the coming days.

Is this split actually the first operation of its kind anywhere in the world?



Indeed it is. I studied the specialist literature in order to learn more prior to the operation, and I really did not find any mention of splitting a liver between two adults in the case of acute liver failure. I also did not find any mention of a liver split in which the organ recipient was treated using this method despite having an incompatible blood group.

What has been the result of the liver split between two adults for the field of transplantation in the Czech Republic?

We have yet to publish the case. We want to write about it once the two patients are home. In the Czech Republic, I would like to open up a discussion on the theme of liver transplants with partial grafts. We have already made a start; we have transplanted livers for a number of patients after reduction, whereby we have reduced the liver inside the donor's body for them prior to the transplant. As I mentioned earlier, starting this year we have also pursued a programme of splitting livers between adults and children. At the IKEM we always consider this possibility in the case of young deceased donors fulfilling the criteria for splitting a liver. We are not yet in a situation where children die on the waiting list, and they do not wait longer than adults. Far from it, thanks to this technique it is usually the case that we do not have a single child on the waiting list. This is new for the Czech Republic, which, on a personal level, makes me very pleased.

Whether we now move forward and systematically consider transplants for two adults from one liver is a matter for very serious debate. For example, we must discuss the subject of those waiting for liver transplants who, in view of their lower weight, wait longer than adults in the higher weight categories. That said, we must also carefully assess whether, in such cases, waiting longer will lead to worse illness or other risks. It is also necessary to assess the risks of this complicated procedure because in theory there is no guarantee that it will always work out as we wish. During the splitting procedure we could damage one or both parts of the liver and it will no longer be transplantable. This is a procedure that carries huge responsibility. We have to be sure that in such cases we treat those on the waiting list who will be able to make use of a split liver rather than wait for a whole one. We have therefore opened up a series of questions to which answers must be found.