A Simple Method of Orthotopic Liver Transplantation in Dogs

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Orthotopic liver transplantations were performed by one team in 18 dogs using a cuff method to anastomose the portal vein, the suprahepatic vena cava and the infrahepatic vena cava without external or internal shunts. Total and warm ischemic times of donor liver averaged 124 and 32 minutes, respectively. The average occlusion time of the portal vein and the infrahepatic vena cava were 9.7 and 13.9 minutes, respectively. During this time, uncontrolled hypotension, petechiae or hemorrhagic enterogastritis did not develop. Sixteen of 18 dogs survived more than five days, and five dogs lived more than three weeks. The cause of death was not related to the cuff method in any instance. This approach proved to be a technically simple and satisfactory procedure.

A MAJOR CONCERN in orthotopic liver transplantation in animals other than primates is the need for bypass of the portal circulation during the anhepatic phase of the operation. Occlusion of the portal vein for more than 20–30 minutes leads to severe hypotension, hypoxic acidosis, hyperpotassemia, cardiac arrhythmia and death.[1-3] To avoid this hemodynamic disturbance, one or two external venous shunts with or without portacaval anastomosis are created to transport blood from the portal vein and inferior vena cava to the jugular vein during the anhepatic period.[3-6] Unfortunately, these procedures are time consuming and, until expertise is achieved, are commonly wrought with problems such as clotting in the shunt, pulmonary embolism and coagulation changes.

This report is concerned with a rapid method of venous anastomosis which precludes the need for portosystemic shunts. Occlusion of the portal vein and suprahepatic vena cava can be released in about ten minutes and the infrahepatic vena cava in less than 15 minutes. Sixteen of 18 animals operated on using this technique survived more than five days. The method is an adaptation of that described by Welch and his associates in heterotopic canine liver transplantation in 1956.[7] Recently, it has been used for rat orthotopic liver transplantation.[8,9]

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Materials and Methods

Thirty-six adult dogs weighing 8.0–25.0 kg without regard to sex were used for transplantation.

Anesthesia was induced with intravenous thiopental sodium (10–15 mg/kg) and followed by endotracheal intubation. To maintain proper anesthesia, nitrous oxide and a minimum of halothane were used. Arterial and central venous pressures were continuously monitored. Both donor and recipient operations were performed under normothermic conditions by a single team of one surgeon and one or two operative assistants.

The donor was prepared as previously reported.[6] The portal vein and hepatic artery were cannulated and perfused with chilled Ringer's lactate solution. After removal of the liver and careful closure of several phrenic veins, cuffs made from polyvinyl chloride connector (Cobe Laboratories, Lakewood, Col) were applied to both the inferior vena cava and the portal vein. The end of each vein was passed through the cuff and everted over its end. The vein was held in place by a ligature of 2-0 silk placed behind a holding ridge (Fig. 1). Usually, half inch cuffs were used for the suprahepatic and infrahepatic vena cava and 3/8 inch cuffs were used for the portal vein.

The abdomen of the recipient was opened through a midline incision. The suprahepatic and infrahepatic vena cava, hepatic artery, portal vein and bile duct were prepared as previously described.[6] The left, caudate and right central lobes were then removed to obtain sufficient length of the suprahepatic vena cava for later introduction of the cuff of donor suprahepatic cava (Fig. 2).

The infrahepatic vena cava, the portal vein and the suprahepatic vena cava were clamped in that order. The vena cava was divided below the left hepatic vein, and the portal vein and the infrahepatic vena cava were divided as close to the liver as possible.

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The donor liver was placed in the hepatic fossa immediately after the remnant liver was removed. The intima-covered end of the cuff of the suprahepatic vena cava was inserted in the stump of the recipient suprahepatic vena cava and doubly tied with 0 silk behind two holding ridges. At this moment, care was taken to see that neither vein was twisted. The portal vein was connected in the same manner and then declamped. About 50 ml of blood was allowed to bleed from the infrahepatic vena cava of the liver in order to avoid air embolism. The clamp on the suprahepatic vena cava was taken off and the infrahepatic vena cava of the donor liver was clamped. Then the final cuff on the infrahepatic vena cava was put in the recipient infrahepatic vena cava and tied. Both clamps of the donor and the recipient side were opened. The donor celiac axis or common hepatic artery and the recipient common hepatic artery were anastomosed with 7-0 or 8-0 silk (end-to-end) (Fig. 3). Finally, the cholecystojejunostomy and jejunojejunostomy were performed (Roux-en-Y).

During the anhepatic period, about 500 ml of the donor blood was administered to maintain arterial pressure.

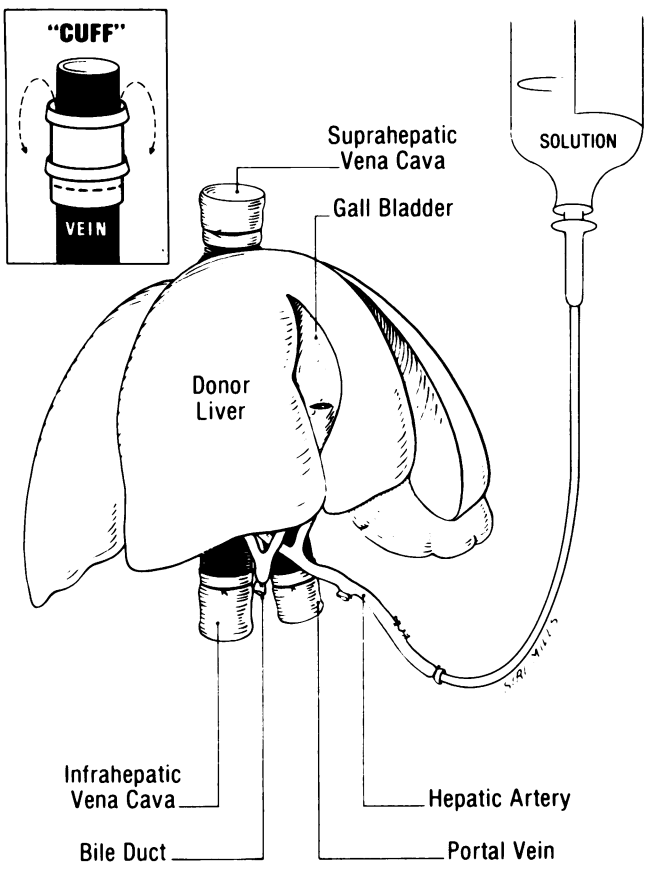

FIG. 1. Preparation of the donor liver. The cuffs are applied on the suprahepatic vena cava, the portal vein and the infrahepatic vena cava.

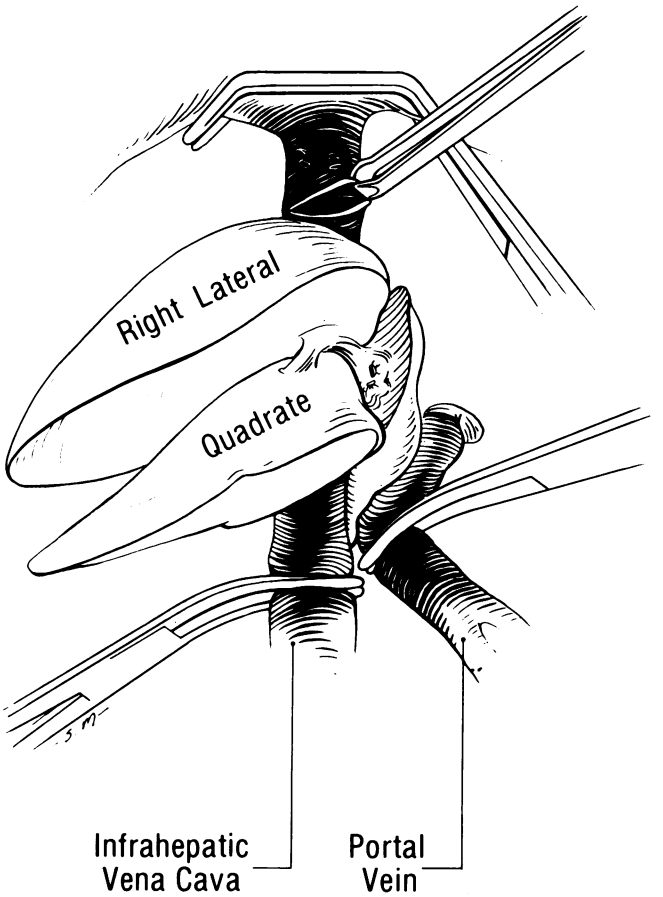

FIG. 2. Preparation of the recipient dog. All left lobes and caudate lobe were removed. The suprahepatic, infrahepatic vena cava, and the portal vein were clamped.

After operation, 0.5 g of cephazolin and 40 mg of gentamycin were administered twice a day for four days. Intravenous fluids including glucose were administered for the first two to three days. In some cases, 4 mg/kg/day of azathioprine or bredinin (10) was given beginning on the day before operation and methylprednisolone, 3 mg/kg/day, was administered beginning on the day of operation and tapered to a dosage of 0.5 mg/kg/day.

Results

Eighteen orthotopic liver allografts were done using the newly established "cuff" method in dogs. The entire operative period was three hours and 30 minutes to five hours and 55 minutes (mean: four hours and 27 minutes). Total ischemic time of the donor liver, from the beginning of perfusion to arterial revascularization varied from one hour and 42 minutes to two hours and 55 minutes (mean: two hours and four minutes). The duration of clamping of the portal vein and the infrahe-

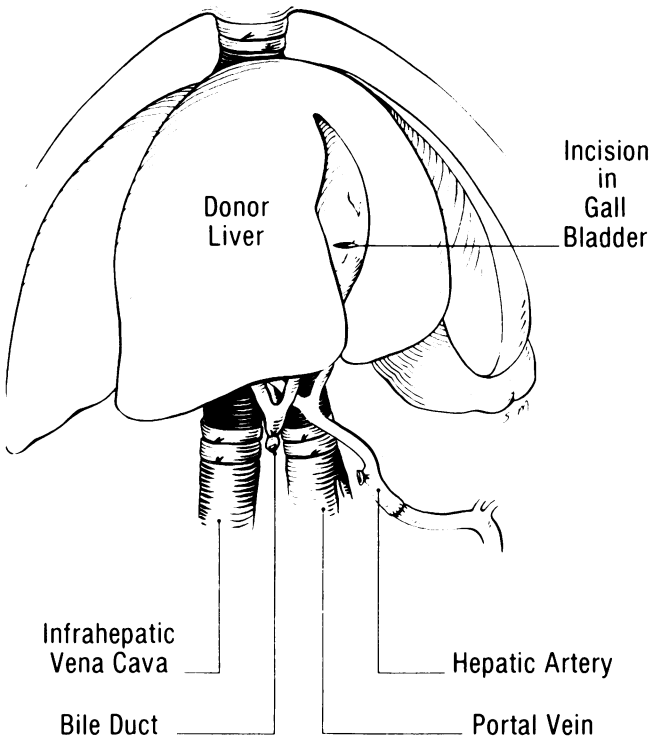

FIG. 3. Diagram of the revascularization.

patic vena cava of the recipient was 8–14 minutes (mean: 9.7 minutes) and 9–22 minutes (mean: 13.9 minutes), respectively.

In the recipient operation, no significant change occurred before the portal vein and the inferior vena cava were clamped, even though about 70% of the liver was removed. At this time the arterial blood pressure was usually between 120 and 140 mmHg. This arterial pressure dropped to about 65% of the initial pressure immediately after the infrahepatic vena cava, portal and suprahepatic vena cava were clamped and the remaining liver was removed. It continued to drop slowly thereafter until circulation was re-established. At the end of the portal vein anastomosis, the systemic pressure varied for 40 to 90 mmHg (mean: 62.7 mmHg, 46.5% of the initial pressure). However, the systemic pressure recovered to the range of 80–140 mmHg (mean: 101.7 mmHg, 77.1% of the original pressure) as soon as the clamps were removed from the portal vein and the suprahepatic vena cava. The blood pressure reached 95% of the original level when the anastomosis of the infrahepatic vena cava was completed and declamped. No major change was observed during and after the arterial anastomosis. Once the portal vein and the suprahepatic vena cava were declamped, the liver regained its color. Its appearance returned to normal following arterial revascularization. The dogs were usually awake on the operating table soon after cessation of anesthesia. They stood up in two or three hours following transplantation.

Sixteen of the 18 dogs survived more than five days. The remaining two dogs died within 24 hours and 48 hours after operation. The former was an early case of this series and the cause of death was not clear. The latter's cause of death was accidental fluid overload. Five dogs died within 10 days of grafting. One dog died, on day 5, of arterial thrombosis, another two died on day 6, one of perforation of a gastric ulcer, and the other of intussusception. Two animals died on day 8 and 9 because of acute rejection. The remaining 11 dogs survived more than 10 days, varying from 11 to 44 days. The main causes of death in these dogs were infection, perforation of gastric ulcers, malnutrition and rejection.

Although the anastomosis was carefully examined at autopsy examination to see if there was some reaction to the foreign body "cuff" and also to see if there were clots or stenosis in the anastomosed vessels, no significant abnormalities were found. There was no evidence to suggest that death in any animal was related to the use of the cuff method.

Discussion

Since Moore and Starzl reported, independently, successful orthotopic canine liver transplantation, there have been many papers dealing with methodology. These papers basically follow the techniques of these two pioneers, which consist of two external venous shunts from the portal vein and the infrahepatic vena cava to the jugular vein in Moore's Method[3,4] or an external venous shunt from the femoral vein with a temporary side-to-side portacaval anastomosis in Starzl's Method[5] during the anhepatic period. These external shunts are both complicated and troublesome because they often result in clotting in the shunt, pulmonary embolism or postoperative hemorrhage when an anticoagulant therapy is employed. In order to avoid these problems, some investigators have advocated methods without caval interruption.[11,12] The resulting survival rate, however, had not improved when compared with survival using the standard shunt method.

In this study, we used the cuff method for anastomoses of the portal vein, the suprahepatic vena cava and the infrahepatic vena cava in order to shorten the time of the clamping of these three veins. The time required for each anastomosis was two minutes or less. The occlusion of the portal vein and the suprahepatic vena cava could be released in an average of 9.7 minutes, and the infrahepatic vena cava was declamped in another 4.0 minutes. During the anhepatic period, arterial blood pressure was quite low, but was usually maintained higher than 60 mmHg by giving about 500 ml of donor whole blood. The decreased pressure returned to normal range soon after the three anastomoses were completed. Uncontrollable hypotension, petechiae

on the bowel or mesenterium or hemorrhagic enterogastritis were not seen.

Another major difficulty in liver transplantation is great susceptibility to anoxia of the canine liver. Welch and associates showed in their heterotopic liver transplantation model that the liver did not survive if kept avascular in normothermic condition for more than 30 minutes.[7] Subsequent investigators have emphasized cooling the liver. When the liver is rendered hypothermic by means of intraportal perfusion with chilled lactated Ringer's solution, an anoxic interval of 75–120 minutes is well tolerated. Introduction of a preservation fluid (plasma-bicarbonate-glucose-procaine) further extends the tolerable period to 180–210 minutes.[13] Initially, we kept the donor liver *in situ* after it was freed except for the blood vessels until the recipient was prepared so that anoxic time was minimized. However, in order to make the procedure simpler, we removed the donor liver first and then prepared the recipient while the donor liver was receiving cold lactated Ringer's solution through a hepatic artery catheter. Using this method, the ischemic time ranged from 79 to 175 minutes with an average of 124 minutes. All transplanted livers tolerated this insult well. One big difference between this method and previously described techniques[3-6,14] is the short time necessary to revascularize the donor liver. The portal and arterial blood supply were resumed in an average time of 9.1 and 32.9 minutes, respectively, after the liver was placed in the recipient abdomen. Warm ischemic time was significantly reduced and outflow block[5] was not encountered.

While the method described is a quick one for vascular anastomosis, it also has other merits. Bleeding from an anastomosis, the most common complication in liver transplantation, is very unlikely to occur. The method rarely causes a thrombosis if the procedure is performed properly because it anastomoses vessels by intima to intima contact. Stenosis at the anastomosis is also avoided. The method has been successfully applied to porcine liver transplantation in our laboratory. This method may be useful for clinical orthotopic liver transplantation.

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