massive infarction and fulminant allograft failure. The biliary tree, however, behaves as a hollow viscus. Ischemia produces a spectrum of injury ranging from mucosal slough to full-thickness necrosis and perforation. Full-thickness necrosis can also produce stricture formation. This appears to be the explanation for intrahepatic stricture formation.

Our experience suggests that percutaneous dilation and stenting is effective therapy for most symptomatic intrahepatic strictures and for strictures of a CDJ anastomosis. It was the only therapy needed in 11 of 17 patients so treated. Three patients developed portal-biliary fistulas, one of whom eventually succumbed. This stresses the need for a radiologist who is experienced in biliary tract interventional procedures. It also emphasizes the need to restrict such procedures to patients who can potentially benefit. In patients with multiple intrahepatic strictures due to hepatic artery thrombosis, retransplantation is probably the treatment of choice (Fig. 5).

Conclusions

From our review of biliary strictures complicating liver transplantation, we conclude that (1) anastomotic strictures are quite rare, (2) the development of biliary strictures may signify occult hepatic artery thrombosis, (3) percutaneous dilation is effective for most strictures, and (4) extended cold graft ischemia (>12 hours) may be injurious to the biliary epithelium, resulting in intrahepatic stricture formation.

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DISCUSSION

DR. G. KLINTMALM (Dallas, Texas): Mr. President, members and guests: This is a very important paper and certainly the biggest series of these kind of problems documented outside Pittsburgh. We have a very similar experience at Baylor with a low complication rate from strictures. We have found that if we divide the strictures up into early—that is, those less than 3 months and those later than 3 months, we end up with two distinct populations.

The early ones are anastomotic, and are in our experience usually due to the training of our fellows. That is where we pay our dues. The second population, which is the larger one, are intrahepatic strictures, and they are, like here, seemingly ischemic in nature. In our experience, two thirds of them are ischemic, and the other third is maybe due to rejection. I have two questions for Dr. Colonna.

This remarkably low incidence of biliary strictures in liver transplantation is worth discussing. Is this due to the steroid therapy we give our patients? As we all know, patients on steroid therapy develop very small scar formations. Should we recommend steroid therapy for all biliary reconstruction to prevent stricture formation also in the nontransplant?

And the second question is, do you have any experience with the indwelling self-expanding Gianturco stents?

DR. HENRY A. PITT (Baltimore, Maryland): I would like to compliment the authors on an excellent series with remarkable results and to comment on both the incidence and management of these strictures.

The incidence is remarkably low, and one of the questions that has to be asked is, why? Do you think that immunosuppression may be playing a role in preventing strictures? As the immunosuppressive regimen has changed over the years, have you noticed a different incidence with one regimen compared with another?

Another possible factor is age. You have a number of children in your series, although they tend to have more choledochojejunostomies. Can you separate these two factors and determine whether the incidence of strictures is related to age?

Another factor that has been debated for years is the length of stenting. You stated that the choledochocholedochotomies were generally stented for 3 to 4 months. Do you have enough range in your length of stenting to determine whether this is a factor in subsequent stricture formation?

The low incidence of strictures that you have reported may be related to the denominator. You seem to have used all of your transplants as the denominator, but not all of your patients are alive at 1, 2, and 3 years. What would the stricture rate be with the denominator being the number of patients alive at two and a half years, your mean length of follow-up?

Another issue that has been debated in the literature has been the definition of success in managing these patients. In some of the radiologic and endoscopic literature, success means that the patient does not require surgery regardless of the need for further nonoperative procedures. In the surgical literature, success is usually defined as a patient who is free of symptoms and has no need for further procedures. What was your definition of a successful outcome?

Again, with respect to incidence, the length of follow-up is very important. Some strictures will not become apparent clinically for 20 years. At two and half years, fewer than two-thirds of the strictures will have presented. Clearly, these patients need to be followed longer to determine the true incidence of bile duct stricture.

Another question relates to patient management. Most of your stricture patients have undergone percutaneous balloon dilatation. Other options include endoscopic balloon dilatation or surgery with or without stenting. Would you comment on these other management options as well as on your use of stents in these patients?

DR. BYERS W. SHAW, JR. (Omaha, Nebraska): This is one of those subjects that in liver transplantation we tend to revisit fairly constantly. There have probably been more papers written about this subject in the field of liver transplantation than about almost any other, with the possible exception of hepatic artery thrombosis. This experience is remarkable because of the low incidence of complications, and I think there are some lessons to be learned from that.

I would also like to echo Dr. Pitt's question and say that I think the incidence of stricture formation can depend a great deal on how aggressively one looks for it and also how one defines a significant stricture. For instance, if you routinely do a T-tube cholangiogram, before you remove the T-tube you sometimes see strictures that, from a functional standpoint, never amount to much.

Another question that has been raised is whether or not biliary stricture leads to a higher incidence of rejection. There have been some concerns raised by others that recurring episodes of cholangitis or elevated liver function secondary to biliary strictures have led to a higher incidence of chronic rejection.

I think our own experience wherein we have operated and converted patients to a choledochojejunostomy and seen only temporary improvement in liver function followed by the development of what looks more like chronic rejection goes along with the experience reported by others. I wonder if the group from UCLA has had a similar experience.

DR. ARTHUR H. AUFSES, JR. (New York, New York): I hate to go back to ancient history, but 40 years ago Drs. O'Malley, Whipple, and I reviewed the experience of common duct stricture at the Presbyterian Hospital. In a group of about 75 patients, there were six in whom the injury occurred in the operating room and was immediately recognized and a duct-to-duct repair was done. All six patients did beautifully in a long-term follow-up.

As we look at our own material in the patients in whom the injury is recognized and followed by an immediate duct-to-duct anastomosis or an immediate choledochojejunostomy, the results are really very, very good. Trying to put that into this analogy, these patients by and large are operated on in a clean field without contamination from prior surgery or prior scarring. I therefore would like to ask the authors, is there any relationship between your stricture formation and prior biliary tract surgery or prior shunt surgery?

DR. CHRISTIAN HERFARTH (Heidelberg, Germany): May I comment with our experience in Heidelberg? We have analyzed a series of 74 patients aggressively according to biliary strictures after liver transplantation and we have found in 32% biliary strictures in patients with a liver preservation of more than 12 hours with UW (University of Wisconsin) solution. We did not observe biliary strictures in patients after liver transplantation with preservation of the liver by Euro Collins solution up to 6 hours.

DR. J. O. COLONNA II (Closing discussion): Dr. Klintmalm asked if steroids are responsible for the low incidence of anastomotic strictures, and if so, should we be doing this for all primary bile duct anastomoses. We believe that immunosuppressive agents are at least in part responsible for the low stricture rate. There is experimental evidence in animals that such agents decrease the stricture rate of visceral anastomoses such as ureteroneocystotomy in rats. We believe it would be entirely appropriate to undertake a prospective, randomized study to compare the addition of steroids to no steroids in patients who have a biliary anastomosis. Dr. Klintmalm also asked if we had any experience with the use of expandable internal stents in managing biliary strictures. To date we have used this type of stent in only one patient. The result was excellent, and we anticipate using this modality more frequently in the future.

Dr. Pitt had several comments. We agree that the stricture rate is somewhat underestimated in that the denominator includes all patients undergoing transplantation, including those who died early after transplantation and therefore may not have lived long enough to develop a stricture. If you consider only those patients with at least 1 year of follow-up, the incidence of stricture would increase to 1%. The mean follow-up for our series was 2.4 years. It was noted in the series from Dr. Csendes in Chile that 75% of strictures were diagnosed within 18 months after a duct-to-duct repair in the nontransplant setting. Our experience has been similar in the transplant setting, and we doubt that longer follow-up will appreciably change the incidence of anastomotic strictures. Dr. Pitt also inquired as to the length of time we leave the stents in place. This is something we are still working out at our institution. We are leaving the stents in place for about a month and removing them if cholangiography demonstrates no restricture. Dr. Pitt noted that in the nontransplant literature comparing operative with nonoperative management of biliary strictures, success is defined as no need for further intervention. In this series, we have defined success as the maintenance of normal graft function. Most patients managed with percutaneous dilation have required repeat dilation, with an average of 2.3 per patient. We have had no experience with endoscopically directed dilation of biliary strictures. Finally, Dr. Pitt asked that I summarize our experience with operative revision. Three patients underwent revision of a CDCD to a CDJ and three patients underwent revision of a CDJ anastomosis. In each case, the operation was successful in relieving biliary obstruction. In two cases the patient died after operation of pre-existent sepsis.

Dr. Shaw noted that the reported incidence of biliary strictures in our paper and in others is probably a product of just how hard you look for them. Clinically silent strictures in the distal biliary radicals may well go undetected. We routinely obtain a cholangiogram at 3 to 4 months at the time of T-tube removal. After that period, cholangiography is only performed when a biliary complication is suspected. Thus the incidence of strictures anywhere in the biliary tree is probably higher, the incidence for clinically significant strictures is quite low. Dr. Shaw also asked about the relationship between frequent episodes of cholangitis associated with biliary strictures and the subsequent development of chronic rejection.

It has been suggested that frequent episodes of cholangitis associated with manipulations of the strictures may lead to an increased expression of class II antigens and may lead to the development of chronic rejection. There were two such patients who developed chronic rejection approximately 12 months after initial diagnosis of the strictures, which were managed with repeated percutaneous dilations.

Dr. Aufses reminded us of a series of six patients, reported by himself and Dr. Whipple, who underwent immediate repair of an accidental bile duct transection with excellent results. More recently a similar series of eight patients has been reported by Dr. Bowden et al., with identical results. In the two largest series to date, however, the results are considerably worse. This is perhaps due in part to the inclusion of patients who underwent their repair at smaller community hospitals before presenting to a large referral center. Dr. Aufses also noted that in general the results seemed to be worse in patients who had undergone other upper abdominal surgery or in whom the injury occurred in the face of a local inflammatory process. He asked if the incidence of CDCD stricture were higher in transplant patients with similar risk factors. Of the three patients in our series with stricture of a CDCD, only one patient had undergone previous upper abdominal surgery, a cholecystectomy.

Finally, Dr. Herfarth reported that their center also has identified a relationship between prolonged cold ischemia time and the development of intrahepatic biliary strictures. Similar to the report by the Mayo Clinic group, he has observed this relationship with both University of Wisconsin (UW) solution and with Euro-Collins solution. We, however, did not see this entity before our use of UW and extended cold ischemia times.