Patients Seeking Liver Transplant Turn to China: Outcomes of 15 Egyptian Patients Who Went to China for a Deceased-Donor Liver Transplant

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Abstract

Objectives: **Increasing numbers of Egyptians with end-stage liver disease seek liver transplants in China because of lower costs and shorter wait times. We evaluated outcomes of Egyptian patients who underwent liver transplants in China and address ethical concerns.**

Material and Methods: **Fifteen Egyptian patients (11 men, 4 women; mean age, 52 years) who underwent liver transplants in China were included. Preoperative data before traveling to China, reports from China, and follow-up data upon return were reviewed.**

Results: **Indications included hepatitis-C–related liver cirrhosis (n=9), hepatitis-C–related liver cirrhosis with hepatocellular carcinoma (n=4), and hepatitis-B–related liver cirrhosis (n=2). Nine patients were evaluated for living-related liver transplant but none of their potential donors was suitable. Three patients had advanced hepatocellular carcinoma and were not accepted for living-related liver transplant by any Egyptian center. Two patients had no living-related donor. One patient refused a living-related liver transplant in Egypt and elected to get a whole liver graft from China. Overall survival rate was 80.0% at 6 months and 73.3% at 12 months. There were 4 deaths; 2 occurred in China. Of the 11 surviving patients, 9 (82%) developed complications. Nineteen complications were seen in the 13 patients who were managed after returning from China. Major complications necessitating prolonged hospitalizations occurred in 4 patients. Two patients required further laparotomy.**

Conclusions: **Although deceased-donor liver transplant in China could be an option for Egyptian patients with end-stage liver disease, patients and clinicians should be aware of potential outcomes and related ethical issues.**

Key words: *Ethics, Organ trading, Moral issues*

Liver transplant is the only effective treatment for end-stage liver disease. In Egypt, living-related liver transplant is the only available option for such patients. Many patients, however, do not have a suitable living donor. The option to go abroad for a deceased-donor liver transplant would attract several patients who cold afford its costs.

Increasing numbers of patients from all over the world including Southeast Asia, North America, Europe, and Australia travel to China for organ transplants. It is said that a liver transplant in China is more affordable when compared with the costs of medical care in the United States and Europe. At the same time, it is possible to get an organ in China in a relatively short time (1). The exact number of Egyptian patients seeking liver transplants in China is not known. This study sought to evaluate the outcomes of deceased-donor liver transplants for Egyptian patients undergoing the procedure in China and addressing ethical concerns.

Patients and Methods

Data of 15 Egyptian patients who had undergone a liver transplant at hospitals in China were retrospectively reviewed. Data included the patient

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Table 1. Patient demographics, disease indications, duration of follow-up, and current status

Patient No.	Sex/age, y	Disease indication	City/costs of surgery, USD $		Follow-up in Egypt	Current status
1	M/51	Hepatitis C cirrhosis	Tianjin	40,000	-	Died in China
2	M/41	Hepatitis C cirrhosis	Shanghai	50,000	-	Died in China
3	M/63	Hepatitis C cirrhosis hepatocellular carcinoma	Tianjin	45,000	4 months	Died in Egypt
4	F/53	Hepatitis C cirrhosis	Tianjin	45,000	21 months	Alive
5	M/65	Hepatitis C cirrhosis	Tianjin	45,000	18 months retransplantat in China	Alive, pending
6	M/47	Hepatitis C cirrhosis	Tianjin	45,000	16 months	Alive
7	M/44	Hepatitis C cirrhosis	Hangzhou	50,000	15 months	Alive
8	M/46	Hepatitis C cirrhosis	Shanghai	60,000	13 months	Alive
9	M/54	Hepatitis C cirrhosis, hepatocellular carcinoma	Beijing	70,000	10 months	Alive
10	F/57	Hepatitis B cirrhosis,	Shanghai	60,000	8 months	Died in Egypt
11	F/47	Hepatitis C cirrhosis	Tianjin	60,000	8 months	Alive
12,	M/49	Hepatitis C cirrhosis hepatocellular carcinoma	Tianjin	60,000	8 months	Alive
13,	M/41	Hepatitis C cirrhosis hepatocellular carcinoma	Beijing	60,000	7 months	Alive
14	F/63	Hepatitis B cirrhosis	Tianjin	65,000	4 months	Alive
15	M/43	Hepatitis C cirrhosis	Shanghai	75,000	1 month	Alive

Abbreviations: M, male; F, female

demographics, disease indications, and the time it took from contacting the Chinese hospital to traveling to China and receiving the liver transplant. In China, data were gathered regarding hospital stay before transplant, the deceased-donor, operative details, and postoperative management including immunosuppression regimens, postoperative complications if any, and duration of stay in China. After coming back from China, follow-up, mortality, morbidity (if any), and current status were assessed. After coming back from China, all patients underwent a full assessment including history, physical examination, laboratory examinations (ie, complete blood count, clotting profile, liver and renal function tests, blood glucose level, hepatitis status, and blood level of immunosuppressants), chest radiograph, and cholangiography if a T tube had been used in situ. The type and dosage of immunosuppressants were reviewed and adjusted.

Results

Of the 15 patients, 11 were men and 4 were women (mean age, 52 years; age range, 41-65 years). Nine of the 15 patients were evaluated for a living-related liver transplant in Egypt. They had family members who had volunteered to be living donors, but none was considered suitable. Three patients had advanced hepatocellular carcinoma and were not accepted by any center in Egypt for a living-related liver transplant (2 had their tumor, 8 and 15 cm, respectively, in the right lobe, and the third one showed evidence of invasion of the main portal vein on triphasic computed tomography). Two patients did not have a relative who could volunteer to donate. The last patient refused the option of having a living-related liver transplant in Egypt and elected to get a whole liver graft from China (Table 1). The indications for liver transplant are shown in Table 1.

Figure 1 shows how to contact a transplant center in China. The first step is usually to call the transplant coordinator of the hospital in China. The

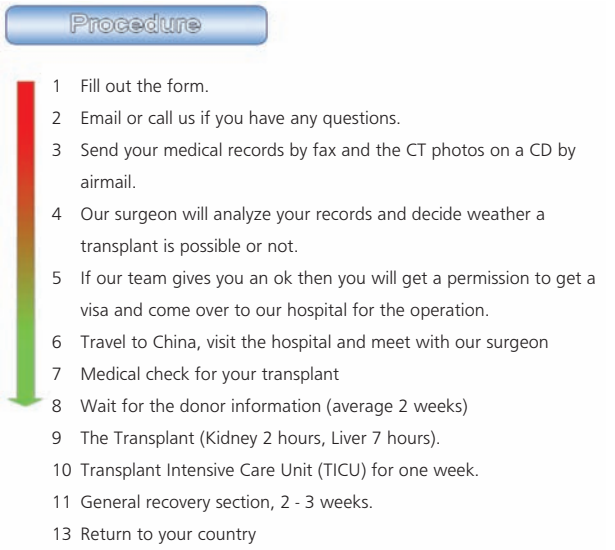

Figure 1. Procedures to get a liver transplant, as mentioned on the Web site of one of the hospitals in China (6)

telephone numbers of these coordinators are easily available on the Web sites of the related hospitals. Most contact persons speak Arabic and English fluently. They can assure the patient or his relative and explain how to proceed and what the expected costs might be.

The length of time from contacting a Chinese hospital to traveling to China ranged from 2 weeks to 6 months (median, 1 month). The costs of surgery range from USD $40,000 to $75,000 (Table 1). The price for patients with blood group O is on average USD $10,000 more than that for other blood groups.

The mean age of the donors was 26 years (age range, 20-34 years; 12 men, 1 woman). The cause of death was severe brain injury in all instances. The median time spent waiting in China before getting a liver transplant was 13 days (range, 5-22 days). The median stay in China was 49 days (range, 28-89 days). Operative details and a pathology report of the explanted liver were either missing or incomprehensible.

Postoperative immunosuppression regimens in all recipients were with triple therapy (ie, methylprednisolone, tacrolimus, and mycophenolate mofetil). There were 2 deaths in China of unknown causes. Only 1 patient had in his report detailed information regarding postoperative morbidity. Patient No. 9 developed methicillin-resistant *Staphylococcus aureus* and enterococcus peritonitis 2 weeks after the transplant, and laparotomy and peritoneal lavage were done in China. Laparotomy showed multiple intra-abdominal abscesses. This patient also developed nosocomial pneumonia after surgery, requiring a temporary tracheostomy and mechanical ventilation, with 28 days respiratory support in the intensive care unit.

The mean follow-up for the 13 patients who returned from China was 9 months (range, 1-21 months). Survival rates were 80.0% at 6 months and 73.3% at 12 months. The mean length of the hospital stay for the 13 patients who returned from China was 41.6 days (range, 4-103 days).

Regarding patient morbidity, there were 19 complications among the 13 patients who returned to Egypt. Two of these patients died of their complications. Four patients developed major complications that required a prolonged hospital stay, and 2 required a repeat laparotomy for drainage of intra-abdominal abscesses. There were 6 instances of infective complications. One patient had de novo hepatitis B after transplant. Another patient had de novo hepatitis C. There were 2 patients who developed pneumonia, and another 2 patients had intra-abdominal, pyogenic abscesses requiring laparotomy and drainage.

Three patients had ischemic bile duct strictures. This was defined as a nonanastomotic intrahepatic biliary lesion with either 2 or more sites of stricture formation and/or biliary dilatation, or multiple intrahepatic fluid collections or abscesses (2).

One patient developed diffuse ischemic biliary stricture and biloma that required percutaneous transhepatic biliary drainage (Figure 2). This patient was repeatedly admitted to the hospital owing to repeated cholangitis that required flushing and revision of percutaneous transhepatic biliary drainage under radiologic guidance. The patient is currently waiting for a repeat transplant in China.

A hepatic artery stenosis occurred in 1 patient, and a partial portal vein thrombosis occurred in another. Both patients presented with abnormal liver function test results; the patients were treated conservatively with anticoagulants. Two patients demonstrated acute cellular rejection as proved by percutaneous needle biopsy. Both were treated with pulse steroid therapy and adjustments of the immunosuppressant therapy. Three patients had reactivation of hepatitis C as proved by elevated liver enzyme levels and quantitative polymerase chain

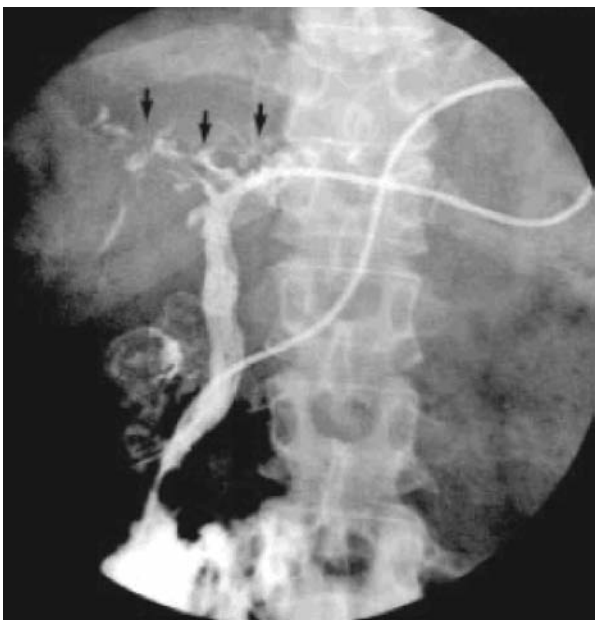

Figure 2. Percutaneous transhepatic cholangiogram of patient No. 5 showing features of diffuse ischemic biliary stricture (arrows).

reaction. Two patients were treated with pegylated interferon subcutaneously every week and oral ribavirin. Both patients showed a satisfactory response.

Two patients died in Egypt. One patient developed a recurrent hepatocellular carcinoma with bilateral pulmonary metastases and died of a severe respiratory tract infection and massive left pleural effusion 8 months after the liver transplant. The other patient had a reactivation of hepatitis C and died of liver failure and sepsis 4 months after the transplant.

Discussion

In Egypt, only living-related liver transplants are done. Many liver transplant candidates do not have a suitable living donor. The option to go abroad for a deceased-donor liver transplant is an attractive option for Egyptian patients who can afford the costs. The question is: What is the best place based on the shortest waiting time, the highest success rate, and the best accessibility for foreign patients. Besides their high costs, the United States and Europe have tight regulations on organ transplant programs to ensure the supply of organs for native citizens first. In contrast, Asian countries have more liberal regulations (3). China has made great strides with transplant surgery in recent years; the number of deceased-donor liver transplants undertaken in China has increased (4). The exact number of Egyptian patients traveling to China for liver transplants is not known; however, it seems that their number is rising. Patients are attracted by comparatively lower costs, shorter wait times, and the idea that they can get a whole liver instead of partial one without the need to look for one or submit one of their relatives to major surgery.

This study reported the outcomes for 15 Egyptian patients who received deceased-donor liver transplants in China. The information accompanying these patients and their donors was not always comprehensive. Information regarding the status of the donor and the condition of the explanted liver, which are crucial for subsequent management and follow-up and for indicating possible complications, were often missing.

Three of our patients who had liver transplants in China for hepatocellular carcinoma and liver cirrhosis were excluded from having liver transplants in Egypt because they had an advanced primary tumor. These patients highlight the differences in selection criteria for transplants in China. In fact, to the best of our knowledge, none of Egyptian patients who sought a liver transplant in China was rejected because of medical reasons. This may reflect the wide and extended indications there. There were 2 hospital deaths; 2 other patients died 4 and 8 months after the transplant. The patient survival rate was 80% at 6 months and 73.3% at 12 months, while 82% of the patients had complications. Surgical complications accounted for 42% of the complications, with biliary complications comprising the majority. Diffuse biliary stricture—as occurred in 3 of the patients in this series (patients 5, 8, and 13)—could have been due to ischemia from a hepatic artery thrombosis or extended graft preservation time and warm ischemic time. It is likely that the occurrence of diffuse, ischemic bile duct strictures in these cases was due to warm ischemic injury to the donor liver during harvesting, because all of the hepatic arteries in these 3 patients were patent on Doppler ultrasound. Information on the process of donor liver graft preservation, and cold and warm ischemic time during these patients' procedures was not available.

Regarding the patients who developed de novo hepatitis B and C, we suspect that the donor liver grafts might have carried the virus. Transmission of hepatitis through transfused blood products is a further possibility in the absence of rigorous blood screening.

Unfortunately, publications from China are not well-indexed in the international literature, and until recently, few papers concerning liver transplants in China had been published (1). It is therefore difficult to access data on a large case series of liver transplants as a comparative standard. One of the rare publications from China (5) reported that between January 2000 and June 2005, one center did 1510 adult liver transplants, all from deceased donors, including 1430 primary transplants and 80 retransplants. The indications were posthepatitis liver cirrhosis (604 cases), fulminant hepatic failure (12 cases), hepatic tumors (892 cases), and traumatic liver failure (2 cases). One hundred seventeen recipients (7.74%) died in the intensive care unit. Four recipients died of a pulmonary embolism during the operation. The overall 1-year survival rate was 87.36% (5).

According to the Web site of the Tianjin First Central Hospital, where 8 of the patients in this study

had their operation: The organ transplant section was founded in 1992. A transplant assistance center, which mainly focuses on foreigners, was founded in 2003. At this center, doctors and nurses are accomplished in English and other languages including Arabic. The center ensures that patients and their families are well taken care of from the time they arrive at the airport until the time they go back to their homeland. Furthermore, lodging, translators, and vehicles are provided to the patients' families; these make the transplant procedure more comfortable and convenient for the patients' families (6).

According to the Korean Organ Transplant Association (7): The number of Korean patients who received transplants in China has sharply increased since 2002 to more than 3000 Koreans in the past 3 years. Lee Poh-hsing, from the National Taiwan University Hospital, (8) reported that hundreds of Taiwanese go to China every year for organ transplants. Some Taiwan doctors are allegedly involved—they introduce Taiwan patients to Chinese hospitals and provide posttransplant care after the patients have returned to Taiwan. The wait time after a regular physical checkup is about 1 week. The 1-year survival rate for a liver transplant was 50% in China compared with 85% in Taiwan. Dr. Poh-hsing supposed that the reason for the decreased survival rate is that the livers were hastily removed from executed prisoners. The Web site of the Changzheng Hospital in Shanghai (where 3 of our patients had surgery) writes, "The average waiting time for a liver supply is 1 week among all the patients" (9). The astonishingly short waiting times for matched organs would suggest the existence of both a computer matching system for transplants and a large bank of prospective donors (8).

In the present study, the cause of death of the donors for all cases was brain injury (as reported by the Chinese Hospitals). The method of execution in China is a gun shot to the back of the head (10); thus, we suggest that all organ donors in this study were executed prisoners. All our patients were told exactly when they should arrive at the hospital, and the organs usually arrived on time. How hospitals meet patient needs so quickly is a question with legal and medical ethical implications, as it may be suggested that execution dates are scheduled to conform with patient transplant needs, rather than to the strict requirements of due process. The death penalty seems to be the basis of China's transplant program. The most important thing is that there is no such "abundant source" of livers anywhere else in the world (8).

The extensive medical practice of liver transplant in China has not appeared in any of the leading international medical journals. The reason for this is thought to be because the source of the organs being transplanted cannot be identified (1).

The Ethics Committee of the British Transplantation Society condemned China's organ harvesting practices as "an unacceptable practice and a breach of human rights" and stated that "an accumulating weight of evidence suggests the organs of thousands of executed prisoners in China are being removed for transplants without consent. The speed of matching donors and patients, sometimes as little as a week, implied prisoners were being selected before execution" (11).

In conclusion, increasing numbers of patients from the world over including Egypt travel to China for organ transplants. The organs are readily available, but the source of "donors" is questionable. Clinicians considering referral of patients to China for deceased-donor liver transplants as well as patients who decide to seek treatment in China should be aware of these ethical issues and the potential risks they may encounter.

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