

Landmarks in Clinical Transplantation in Korea

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HISTORY OF CLINICAL TRANSPLANTATION SURGERY

Since transplantation surgery is not simple, but requires the cooperative work of various academic, laboratory and social fields, pathetical sincere efforts and sacrifices of pioneering surgeons were required. The first renal transplantation (from a 58 years old mother to her 33 years old son), on March 25, 1969, performed by Professor Yong Kak Lee (Fig. 1) and his associates (Catholic Medical College St. Mary's Hospital), aroused the interest of many surgeons,¹ with his team playing a significant role in organizing The Korean Society for Transplantation in December 1969. Professor Yongsook Gee (Catholic Medical College) was elected as the founding president. However, only sporadic cases of clinical renal transplantation and experimental research works on liver and kidney transplantations were performed during the subsequent 10 years following the first renal transplantation. The passion and efforts of pioneering surgeons and physicians could not overcome the poor medico-social environments at that time; and further, the disappointing transplant outcomes. In 1977, the first HLA typing laboratory for transplantation was installed at the Department of Surgery, Yonsei

University Medical Center-Severance Hospital, by Professor Kiil Park (Fig. 2) under the auspices of the Minnesota Transplant Program. In 1979, he started the Severance Transplant Program, as the first step in marking the historical number of more than 2200 kidney transplants in a single center 25 years later. In the same year, although, legally not supported, Professor Jin Young Kwak



Fig. 1. At the St. Mary's Hospital in Seoul, Professor Yong Kak Lee performed the first successful kidney transplantation on March 25, 1969. He is also a pioneering surgeon in the history of vascular surgery in Korea.



Fig. 2. In 1977, Professor Kiil Park installed the first HLA typing laboratory for transplantation in Korea. He activated the donor exchange swap and swap-around program, and has been involved in more than 2200 kidney transplantation at the Yonsei University Medical Center-Severance Hospital. After retiring from Yonsei University in early 2004, he has been serving as the director of the newly-built Kwandong University Myongji Transplant Center.

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(Fig. 3) and his associates (Hanyang University Hospital) performed the first cadaveric renal transplantation under the institutional guideline only.² In 1979, the Korean government initiated the state-run health care system, and in 1988, the provision of health care was extended to include most of the population. The provision of health insurance system, and the introduction of cyclosporine A (CsA) in 1984, provided momentum and encouraged transplant surgeons to expand their clinical experiences of transplantation.^{2,4} In 1988, Professor Soo Tae Kim (Fig. 4) and his associates (Seoul National University Hospital) performed the first successful cadaveric liver transplantation in a patient suffering from Wilson's disease.⁵ Liver transplantation was his long cherished desire after returning from Denver. Later, in 1998, he reported 25 cases of personal experiences of liver transplantation.⁶ During the years 1992-1997, pancreas (including pancreas-kidney), heart, living donor partial liver, lung, heart-lung transplantations were all successfully and independently performed by Professors Duck Jong Han, Meong Gun Song, Sung-Gyu Lee (Fig. 5), Doo Yun Lee and Kook-Yang Park.²



Fig. 3. Professor Jin Young Kwak performed the first cadaveric kidney transplantation on January 13, 1979, and introduced the concept of the living donor kidney exchange program in 1991.



Fig. 4. Professor Soo Tae Kim performed his first kidney transplantation surgery on July 15, 1969, and performed the first successful cadaveric liver transplantation on March 16, 1988.



Fig. 5. Professor Sung-Gyu Lee performed the first living donor partial liver transplantation in a pediatric patient in 1994, and introduced the surgical techniques for adult-to-adult living donor and multiple living donor partial liver transplantation. His team performed 217 cases of liver transplantation in 2003, which is more than half of the liver transplantations reported to the KONOS.

RECOGNITION OF BRAIN DEATH

The declaration of brain death as another manifestation of the cessation of life, and its recognition by The Korean Medical Association in 1993, improved the shortage of organ donors. The declaration made by the most influential and highest level of medical association in the country, while brain death was not accepted legally, demonstrated its acceptance by the medical fraternity. With this approval, medical centers have subsequently been allowed to tacitly use cadaveric organs. After the declaration, the number of cadaveric organs made available increased sharply. As of February 2000, the "Law on The Transplantation of Human Organs" took effect; legally allowing the transplantation of organs from patients declared brain dead. This law laid the groundwork for the prevention of the sale of human organs by intermediaries. The decree stipulates "all the information regarding the donor and recipient will be handled by a centralized national organization, with prospective recipients selected fairly in accordance with medical standards in the designated geographic regions".^{2,4}

THE KOREAN NETWORK FOR ORGAN SHARING (KONOS)

The KONOS, the state-run central agency established by the new law, was launched in February 2000 under the wing of the National

Medical Center in Seoul. Its major responsibility is to manage all the procedures related to transplants, both from brain-dead and live (related or unrelated) donors, on a national basis. The major objectives of the KONOS were to improve the effectiveness of the nation's organ procurement, distribution and transplantation system by increasing the availability of donor organs, to prevent the illicit handling of human organs, collect and analyze the data on procurement, preservation and tissue typing, and to monitor the clinical outcome of transplantation. The KONOS divided the nation into three large geographical regions. Basically, organs removed from the deceased in one region must be transplanted to patients in the same region. Hospitals have to obtain licenses from The Ministry of Health and Welfare if they want to perform organ transplants. Those hoping to donate or receive human organs are required to register and get permission from the KONOS.^{3,4}

EFFORTS TO PROMOTE ORGAN TRANSPLANTATION

As of the end of 2001, 31,014 patients were dependent on various kinds of renal replacement therapy. Of these, 25.7% are enjoying the benefits of transplantation. In 2001, 5500 new patients requiring renal replacement were reported, but renal transplantations were performed in only 15.4%.⁴ The principle cause for this disparity was the absolute shortage of kidney donors. In Korea, live related transplants have been considerably more common than cadaveric ones for a variety of reasons. In the absence of legal recognition of brain death, Professor Jin Young Kwak initiated the live unrelated kidney donor exchange transplant program in 1991, and Professors Kiil Park, Yong Bok Koh (Fig. 6) et al. promoted and activated this program further. These were done to alleviate the shortage of donor kidneys. These programs, unique to Korea, were successful, and were eventually expanded in scope to a multiple donor exchange swap-around program. The indication, process and outcome of these programs have already been published.⁷⁻⁹ Currently, the five-year graft survival in 90 swap recipients from



Fig. 6. Catholic University Kangnam St. Mary's Hospital Transplant Program, directed by Professor Yong Bok Koh, is one of the most successful and long-standing transplant programs in Korea. Currently, Professor Koh is leading the Korean Society for Transplantation as a president.

the Severance Hospital Transplantation Center is 90.6%.⁴ Additionally, to overcome the cross-match barrier in renal transplantation, Professor Soon Il Kim and his associates have used a combination of plasmapheresis, intravenous gammaglobulin and potent immunosuppressions to induce negative cross-match conversion in patients who had a positive cross-match with their living donors at the Severance Hospital.⁹ To overcome the donor shortage in liver transplantation, living donor partial liver transplantation was started, in 1994, by Professor Sung-Gyu Lee and his associates at Ulsan University-Asan Medical Center. Initially, they started in pediatric recipients, but this indication was progressively extended to adult-to-adult from 1997.²

EVOLUTION OF IMMUNOSUPPRESSION

Immunosuppression protocols have changed over the years as new immunosuppressive agents have emerged. Since the introduction of CsA, early in 1984, CsA-based double and triple (including azathioprine) therapies have constituted the major method by which immunosuppression has been maintained. From the late 1980's, cadaveric donor recipients frequently received anti-lymphocyte globulin (ATGam[®] or OKT₃[®], according to the functional status of their grafts for the first 7-10 days. After early 1995, microemulsion CsA (Neoral[®]) replaced conventional CsA for a short period through the nation. However, mycophenolate mofetil (MMF), introduced early in 1997, has slowly been used in preference to azathioprine. The clear benefit of MMF in

Table 1. The Number of Donor-specific Individual Organ Transplants Performed, and Reported to the KONOS from 2001 to 2003 in Korea¹².

Year	Kidney			Liver			Heart	Pancreas
	*CAD	Living	Total	*CAD	Living	Total	*CAD	*CAD
2001	101	690	791	37	286	323	21	5
2002	70	669	739	28	335	363	11	8
2003	124	682	806	50	364	414	15	12

*CAD, Cadaveric.

reducing the incidence of acute rejection, even after living donor kidney transplantation, and the effect and action mechanism of mycophenolic acid on the vascular smooth muscle cells, were demonstrated by Professor Yu Seun Kim, et al. at the Severance Hospital Transplantation Center.^{10,11} After the introduction of tacrolimus in 1999, tacrolimus-based immunosuppression in liver transplants and living unrelated kidney transplants has been used frequently. Basiliximab or daclizumab has been routinely used in second or unrelated donor kidney transplants as an induction treatment.

CURRENT STATUS OF TRANSPLANT OUTCOME AND TRANSPLANT REGISTRY

Most recent transplant statistics from the KONOS are depicted in Table 1.¹² Reviews on the kidney transplantation activities and survival statistics have been already published in the English literature from the Severance Hospital Transplantation Center and the Catholic University Medical Center.^{9,13-16} Nation-wide, the KONOS 3-year graft survivals for cadaveric kidney, liver, heart, and pancreas transplantations have been reported to be 88.1, 68.2, 90.3 and 79.5%, respectively, and the 3-year graft survivals for living donor kidney and partial liver transplantations have been reported as 95.5 and 78.1%, respectively.¹² The high graft survival in the cadaveric recipients might be attributed to the short cold preservation time (less than 12 hours of cold preservation in over 90% of recipients) resulting in injury-free organs.

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