the Pontifical Academy of Sciences

Proceedings of the Workshop on The Role of Science in the Development of International Standards of Organ Donation and Transplantation

Editorial group:

Nancy L. Ascher, Professor and Past Chair, Department of Surgery, University of California, San Francisco, United States. Past President, The Transplantation Society (TTS)

Beatriz Dominguez-Gil, Director General, Organización Nacional de Trasplantes, Madrid, Spain

Efstratios Chatzixiros, Adviser, Transplantation and Products of Human Origin, Department of Health Products Policy and Standards, WHO, Geneva, Switzerland

Francis L. Delmonico, Professor of Surgery, Harvard Medical School at the Massachusetts General Hospital, and Chief Medical Officer, New England Donor Services, Boston, United States. Councilor of the Pontifical Academy of Sciences (PAS) and Chair, WHO Task Force Donation and Transplantation of Organs and Tissues.

Disclaimer: The perspectives expressed during the presentations of this Workshop were given with absolute academic freedom. Although published by the Pontifical Academy of Sciences (PAS), the Proceedings represent only the points of view of the participants and not those of the PAS nor those of the World Health Organization.

Acknowledgment: the enduring support and guidance of PAS President **Joachim von Braun**, PAS Chancellor **Bishop Marcelo Sánchez Sorondo,** WHO Assistant Director-General **Mariângela Simão**, and WHO Director of Department of Health Products Policy and Standards **Clive Ondari**, are gratefully acknowledged. We also express our appreciation to Professor **Alexander M. Capron**, University of Southern California for insightful comments.

EXECUTIVE SUMMARY

Transplantation is the best if not the unique treatment for patients with end-stage organ failure. However, thousands of patients die or endure a poor quality of life (QoL) while waiting for a transplantable organ. The shortage of available organs is also the root cause of organ trafficking and transplant tourism, practices that pose a severe risk to individual and public health and to the notion of national self-sufficiency. Organ trafficking and transplant tourism violate fundamental human rights, as protected in the WHO Guiding Principles on Human Cells, Tissue and Organ Transplantation.

Pope Francis has urged the international community of transplant professionals to address organ trafficking as a crime against humanity. Because combatting organ trafficking requires addressing its root cause, which is the inability of countries to provide for the transplantation needs of patients, **the Pontifical Academy of Sciences (PAS) convened in June 2021, a Workshop for promoting *the Role of Science in the Development of International Standards of Organ Donation and Transplantation*.** The Workshop addressed the following health-care issues:

- Evaluation of the burden of disease that results in organ failure and necessitating organ transplantation for treatment and the need to include transplantation in the treatment continuum as part of universal health-care;
- A compelling case for prioritizing organ transplantation in the treatment of organ failure;
- Technical considerations for developing and optimizing organ transplantation as a health-care treatment option for patients with organ failure; and
- Strengthening the regulatory capacity for oversight of practice.

The Workshop was co-sponsored by the World Health Organization (WHO) and was attended by more than 200 health officials and transplant professionals from 63 countries throughout the world. A panel of renowned international experts comprehensively presented the latest scientific evidence and best practices, analysed the various factors that are relevant in the development of a national transplantation system and suggested common standards.

The Burden of Disease

The burden of disease that results in organ failure is increasing in relation to underlying risk

factors. There is insufficient progress to reverse trends in the burden of these diseases that have a profound social and economic impact on communities and on individuals. The justification for action is strong. Data need to be examined to implement preventive measures, but also to utilize the most cost-effective treatment for patients who are suffering with organ failure and to have access to care through organ transplantation. **Transplantation should be considered in the continuum of care for patients with chronic organ disease, in keeping with pursuit of Sustainable Development Goals 3.4. (premature mortality from non-communicable diseases) and 3.8 (Universal Health-Care).**

A compelling case for prioritizing organ transplantation in the treatment of organ failure: benefits of Kidney and Liver Transplantation

There is a disproportionate worldwide use of dialysis as kidney replacement therapy when compared to kidney transplantation, that cannot be explained when governments consider the survival, QoL and cost-effectiveness advantage of kidney transplantation. Worldwide in 2019, 100,094 kidney transplants were performed, compared to more than 5 million patients undergoing dialysis annually. People with chronic kidney disease experience reduced QoL because of high symptom and treatment burden. Once an individual reaches end-stage renal disease, the treatment modalities are limited to transplantation, hemodialysis and peritoneal dialysis. In all WHO regions, with the possible exception of Africa, hemodialysis is more costly than maintaining a kidney transplant, and this cost difference is widest in high-income countries. **The scientific analysis of cost and outcome data suggests that kidney transplantation should be considered the optimal treatment for renal failure. The current reality that this is not the case in so many countries is unacceptable.**

There is substantial evidence that liver disease is increasing in incidence and is a major source of death and disability in the world. Liver disease affects patients of all ages compromising their life expectancy, QoL and productivity. Liver transplantation is an effective treatment for chronic liver disease, fulminant hepatic failure and hepatocellular carcinoma with excellent short and long-term survival. The alternative to transplantation is death in patients with both acute and chronic liver failure. **Many countries do not have active liver transplant programs** and those newly developed in countries without robust governmental support, generally initiate the programs utilizing living donors. This approach requires extensive surgical expertise and substantial hospital resource and relies on protection of living donors from exploitation. The extensive hospital support often limits activity to private for-profit institutions.

Technical Considerations for Developing and Optimizing Organ Transplantation

The decision to embrace and support transplant activity must be assessed on the background of the community's (country's) burden of disease, loss to the community of productive members and other health obligations. It may be that the community must start with the greatest potential for

benefit (e.g. living donor kidney transplant in place of dialysis therapy or living donor liver transplant for liver cancer). Once the infrastructure is in place and the work force has been developed, transplantation services may be expanded to include deceased donor transplants and the indications widened. **Requirements for the development of a transplant program are: 1) Legislation, credentialing and regulatory oversight; 2) Financing of all aspects from donation to the long-term care of living donors and recipients; 3) Workforce; 4) Interventions and procedures; 5) Laboratory; 6) Medication; and 7) Protocols.** (See Table 1 of the Proceedings pages 20 -21)

The Legislative Framework

Consistent with WHO Guiding Principles, legislation pertaining to donation and transplantation should be adopted to establish a **National Transplant Agency** that provides oversight and coordination of donation and transplantation activities, and the establishment of **registries and a system of traceability and vigilance** to ensure safety (both for donors and recipients), efficacy and quality of organs. Legislation should provide the **legal basis for organ removal from deceased donors**, with the ultimate goal to maximize donations from the deceased. Legal and logistical steps are needed to establish deceased donor programs where these do not exist, and to make existing programs as effective and efficient as possible. Organs should not be removed from the body of a deceased person unless that person has been certified dead in accordance with the law and unless the consent or authorization required by law has been obtained. **A schematic of the minimum health requirements for performing deceased organ transplantation is provided from these Proceedings.** Intensive care professionals should be actively engaged in the development of deceased organ donation programs and the criteria for the determination of death.

The Council of Europe has been actively involved in the elaboration and promotion of legal instruments that aim at harmonizing international legal frameworks to provide concerted and effective efforts to prevent and address **illicit transplantation practices** at international level. The Council of Europe Convention against Trafficking in Human Organs is built around the notion of the “illicit removal of human organs”. This is defined as organ removal: 1) without the free, informed and specific consent from living donors or without valid consent or authorization for deceased donation; or 2) in exchange for financial gain or comparable advantage. Any subsequent action involving illicitly removed organs is also considered to be organ trafficking. By ratifying this Convention, parties show their commitment to preventing and combating these crimes.

Deceased Organ Donation

Well-established deceased organ donation programs are essential components of each transplant system and a prerequisite for achieving self-sufficiency. Life-saving transplant treatments (such as heart transplantation) cannot be developed unless deceased organ donation is established. Lung and liver (kidney as well) transplant programs should rely on deceased donation to avoid the

burden and minimize the risk for living donors. Therefore, national competent authorities should target this goal as a priority when building up transplant programs or optimizing access to transplantation treatment.

Living Organ Donation

Living kidney and liver donation has proven to be safe when performed under an appropriate framework of donor care even though an inevitable small mortality risk is well documented. Transplantation of kidneys from living donors is considered a necessary adjunct today to achieving national self-sufficiency. However, **the national program of organ transplantation should not exclusively rely on living donation.** Governments should not enable rich patients to travel to foreign destinations and undergo kidney transplantation from living donors that are unknown to the recipients. **Registries of living donor transplants** should focus upon the safety and well-being of the living donor. Complications that require re-hospitalization of the living donor should be recorded and so should donor deaths associated with the procedure of organ removal. Thus, registries provide important data to base the donor´s consent on the assessment of known risks (at the specific center, national and international level).

Strengthening the Regulatory Capacity for Oversight of Practice

There is no standard of data collection by responsible national agencies to assess performance of transplant centers and improve patient care for transplant recipients and the living organ donors. Ideally, data should be collected at three levels: internationally (exemplified by the Global Observatory on Donation and Transplantation), nationally and at a center level. National waiting list, donor, recipient and follow-up registries are essential **to achieve and continuously monitor quality, expertise, safety and transparency of all steps of the organ donation and transplantation process.**

Models of evolving and established systems of donor and transplantation practices are provided in these proceedings.

Conclusions

- Organ failure, particularly kidney and liver failure, caused by non-communicable and transmitted infectious diseases are exponentially increasing throughout the world;
- The cost of caring for these patients exceeds many other disease entities;
- Organ transplantation as a treatment provides the best survival and QoL with a cost efficiency. The “cost efficiency” issue may not be the case in the poorest countries, but can only be determined with the acquisition of accurate burden of disease data;
- The cost of inaction is substantial given the impact of organ failure upon individuals, and the

social and economic impact of diseases leading to organ failure on communities;
- Governments must address national self-sufficiency by developing systems that provide organs for their patient population via living and deceased organ donation;
- National self-sufficiency requires a legislative framework that includes oversight of a national agency;
- The Workshop provided operational guidance of ethically sound living and feasible deceased donor transplantation including a mandated collection of data pertaining to safety of the living donor and outcome measurements for the recipients;
- International cooperation (financial, exchange of best practices, and provision of technical expertise) is required to support countries in progressing towards self-sufficiency in transplantation, particularly to low resource countries;
- The development of effective transplant systems is the fundamental means to prevent organ trafficking and protect the vulnerable from exploitation.