



Benchmark center volume and regional disparity in living donor liver transplantation

Ivan Vella^{1^}, Fabrizio di Francesco^{1^}, Sergio Li Petri¹, Duilio Pagano^{1^}, Caterina Accardo^{1^}, Giuseppe Mamone^{2^}, Sergio Calamia^{1^}, Salvatore Gruttadauria^{1,3^}

¹Department for the Treatment and Study of Abdominal Diseases and Abdominal Transplantation, Istituto di Ricovero e Cura a Carattere Scientifico-Istituto Mediterraneo per i Trapianti e Terapie ad alta specializzazione (IRCCS ISMETT), University of Pittsburgh Medical Center Italy (UPMCI), Palermo, Italy; ²Radiology Unit, Diagnostic and Therapeutic Services, Istituto di Ricovero e Cura a Carattere Scientifico-Istituto Mediterraneo per i Trapianti e Terapie ad alta specializzazione (IRCCS ISMETT), University of Pittsburgh Medical Center Italy (UPMCI), Palermo, Italy; ³Department of General Surgery and Medical-Surgical Specialties, University of Catania, Catania, Italy

Correspondence to: Salvatore Gruttadauria, MD, PhD, FACS. Chairman of the Abdominal Center Department, Department for the Treatment and Study of Abdominal Diseases and Abdominal Transplantation, Istituto di Ricovero e Cura a Carattere Scientifico-Istituto Mediterraneo per i Trapianti e Terapie ad alta specializzazione (IRCCS ISMETT), University of Pittsburgh Medical Center Italy (UPMCI), Via Ernesto Tricomi 5, 90127 Palermo, Italy; Department of General Surgery and Medical-Surgical Specialties, University of Catania, Catania, Italy. Email: sgruttadauria@ismett.edu.

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In the current scenario of modern transplantation medicine, and thanks to the improved outcomes of liver transplantation (LT) in adult patients, the number of transplants performed is increasing, though the gap between organ demand and supply persists (1).

Over the years, the indications for transplantation have been expanded, demonstrating the efficacy of LT even in the emerging field of transplant oncology, as is the case with liver metastases from colorectal cancer and cholangiocarcinoma.

In the face of such an increase in the demand for organs, transplant centers around the world have been looking for ways to expand the donor pool. In the context of deceased donation, much has been done to increase the utilization rate of these organs. Enormous progress has been made with the use of perfusion machines, which in some cases have been able to prolong organ ischemia time, if not

recondition marginal organs, improve outcomes after LT, and allow viability assessment before transplantation (2). In addition, normothermic regional perfusion (NRP) of donation after circulatory death (DCD) donors has dramatically increased the number of donors, especially in European countries (3).

Living donor liver transplantation (LDLT) is also an important resource for expanding the donor pool, shortening the waiting list, and reducing recipient mortality. Despite the deployment of all these strategies, globally, demand for organs far exceeds supply. The unfortunate consequence of this mismatch is the high waiting list mortality rate, which in the United States reaches approximately 13% of patients listed for LT (4).

While LDLT was initially established for pediatric recipients in the mid-1990s, the last two decades have seen a resurgence of this type of donation in the adult recipient

[^] ORCID: Ivan Vella, 0000-0002-4946-512X; Fabrizio di Francesco, 0000-0003-3473-2544; Duilio Pagano, 0000-0003-3987-9262; Caterina Accardo, 0000-0003-3497-683X; Giuseppe Mamone, 0000-0002-5100-463X; Sergio Calamia, 0000-0002-8594-0071; Salvatore Gruttadauria, 0000-0002-9684-8035.

population. LDLT is undoubtedly much more prevalent in Asian countries than in Western countries, due to lower rates of cadaveric donation. Globally, the volume of LDLT has increased sharply, and even the geographical distribution has changed: in 2022, nearly two-thirds of LDLT were performed in India (35%), Turkey (16%), and South Korea (12%) (5). In Canada, the rate of living donation is the highest among Western countries, with approximately 15% of all transplants performed; however, in the United States, according to the latest published data, living donation accounts for only 6.2% of total donations, while the figure is even lower in the United Kingdom and Italy, where it reaches only 2% (4,6). As mentioned above, this proportion is completely different in Asian transplant centers, where living donation reaches 90% of the total (7). These data can be explained by the fact that Asia, in contrast to the Americas and Europe, is characterized by a diversity in terms of social, economic, and cultural factors.

Recently, Li and colleagues reported an interesting paper entitled “Novel Benchmark for Adult-to-Adult Living-donor Liver Transplantation: Integrating Eastern and Western experiences” (8). In this paper, the authors analyzed and defined the benchmarks for LDLT in adult patients. They studied a large population of patients undergoing LDLT in 15 high-volume centers (at least 10 cases per year), including at least three countries, over a 5-year observation period with at least one year of follow-up. A total of 1,864 patients were qualified as benchmark cases with the following characteristics: absence of portal vein thrombosis, laboratory Model for End-stage Liver Disease (LabMELD) ≤ 20 , absence of renal failure requiring pre-transplant replacement therapy, absence of previous major abdominal surgery and, finally, absence of acute liver failure or intensive care unit (ICU) admission before LT. The majority of grafts procured were right hemi-liver grafts (88.3%), and the median LabMELD score was 12 (interquartile range, 9–16).

The results of this analysis reported benchmark cutoffs one year post-LT as follows: post-LT renal failure requiring replacement therapy ($\leq 4\%$), primary non-function ($\leq 0.9\%$) and graft loss ($\leq 7.7\%$), non-anastomotic biliary strictures ($\leq 0.2\%$), and need for retransplantation ($\leq 3.6\%$) were below the homologous benchmarks for deceased donor LT (9–11). Bile leak ($\leq 12.4\%$), hepatic artery thrombosis ($\leq 5.1\%$), and Comprehensive Complication Index (CCI[®]) (≤ 56) were above, and all-cause mortality ($\leq 9.1\%$) was comparable. The right hemi-liver graft was characterized by a lower CCI[®] score compared to the left hemi-liver (34 *vs.* 21, $P < 0.001$).

The authors then compared the outcomes among centers with different volumes, showing a clear benefit in the high-volume centers performing at least 10 cases per year.

The choice to preserve the middle hepatic vein with the right hemi-liver graft had no impact on the post-operative outcome for either donor or recipient. Asian centers outperformed other centers, with statistically significant differences, in terms of lower CCI[®] score (21 *vs.* 47), lower rate of graft loss (3.0% *vs.* 6.5%), and consequently, a lower rate of redo-LT (1.0% *vs.* 2.5%). At the same time, Asian centers reported longer recipient surgical time, longer ICU stay, and longer hospital stay.

Indeed, the choice between the right and left hemi-liver is an important point of debate in the literature. Though a recent meta-analysis showed that right hemi-LT is safer for the donor, with no difference in outcome for the recipient (12), the study by Li and colleagues revealed a different picture. It found worse outcomes in left hemi-LT, both in terms of more severe complications (higher CCI[®] score) with longer ICU and hospital stays, and a higher risk for recipients of developing small-for-size syndrome. The authors conclude that preference should be given to the right-hemi-liver graft. On the donor side, a recent Chinese report of 380 adult LDLTs by Wang and colleagues (13) showed how the left hemi-liver remnant had a faster growth rate than the right hemi-liver remnant, reflecting the high regenerative capacity of liver tissue in healthy individuals. In our opinion, donor safety must always come first, and we still believe that the right hemi-liver remains the best choice whenever possible.

Our center's experience with right lobe LDLT (RLDLT) was reported in a recent review (14). Our LDLT program started in 2002, and a total of 112 RLDLTs were performed by 2023, with excellent results. The program experienced a significant initial surge, with 90 cases completed between 2002 and 2010, followed by a sharp decline. This post-2010 decline reflects the broader trend of reduced LDLT procedures in the Western world, largely due to reports of serious complications in a small number of donors. Notably, in 2012, the first European and second worldwide robotic-assisted living donor right lobe procurement for LT was performed in collaboration with the University of Pisa, in Italy, following the pioneering case by Vella and colleagues the previous year (14). Interestingly, of the 17 RLDLT cases performed from 2013 to 2023, six took place in the last 2 years (2022 and 2023), suggesting a resurgence in the program. A recent report has shown that RLDLT in patients with low MELD scores significantly reduces the

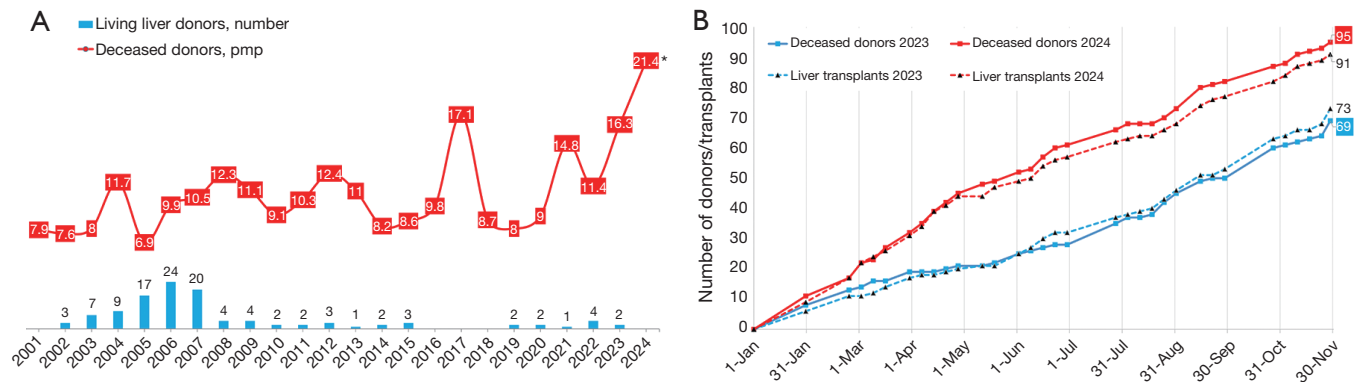


Figure 1 Recent increasing trend in organ donation in Sicily. (A) Trends in organ donation over time from both deceased donors (reported in number of donors per million population) and living donors (reported in absolute numbers). (B) Comparison of regional deceased donors and liver transplantations on adult recipients between 2023 and 2024. Data about donors are courtesy of the Italian National Transplant Center. *, the figure for 2024 is a projection made from data available as of November 24, 2024. pmp, per million population.

risk of dropout, making it an important tool for expanding the donor pool (15). In 2023, Italy recorded a 15% increase in the number of LT compared to the previous year (1,701 LTs performed), but only 39 of these were LDLTs (6).

In the current year, 2024, a further 20% increase in deceased donation and a consequent higher number of LTs performed has brought to light a new scenario in which LT programs have a shorter waiting list, and with faster turnover.

The increased donation rate in our region, Sicily, which until 18 months ago was characterized by low rates of deceased organ donation and widespread opposition to donation, has led to a change in the numbers, resulting in 100 LTs performed in 1 year (*Figure 1*). As a result, this has led to a change in the attitude of patients and their family members toward receiving a deceased donor graft.

In conclusion, LDLT represents a crucial resource for addressing the organ donation deficit in both Asian and Western countries. The recent work of Li and colleagues has demonstrated the safety of the technique for both the donor and the recipient, as well as its capacity to achieve excellent results. However, it is imperative that this procedure be performed exclusively in centers with extensive experience in this type of surgery, with a strong emphasis on centralizing these types of patients to the greatest extent possible.

These findings indicate a necessity for the establishment of a network between high-volume centers and those with a limited number of cases per year, with the objective of attaining optimal outcomes.

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