EJT European Journal of Transplantation

2023;1:4-12
DOI: 10.57603/EJT-003

Original article

MACHINE PERFUSION IN ITALY. THE EVOLUTION OF THE CLINICAL PRACTICE

Silvia Trapani, Francesca Vespasiano, Lucia Masiero, Francesca Puoti, Silvia Testa, Pamela Fiaschetti, Daniela Peritore, Alessandra Oliveti, Francesco Procaccio, Massimo Cardillo

Italian National Transplant Center, National Institute of Health, Rome, Italy

Summary

The use of extended criteria donors (ECD) became widespread due to the shortage of organs available for transplantation. The use of *ex-situ* machine perfusion (MP) after organ retrieval is strongly recommended in this field, to improve clinical outcomes following transplantation. Adopting MP strategies requires huge financial resources that can only be optimized if MP is introduced more widely, with evidence of significant benefits.

Objective. 1) to evaluate the evolution of MP use in Italy over the time and its potential impact on the organ pool available for transplantation; 2) to measure the quality of the MP program.

Methods. The "Methods of organ perfusion in transplantation" was adopted in 2017, including recommendations for implementing a national program; a database was set up to collect the data of *ex-situ* perfused organs, procured from DCD or DBD donors.

Results. The *ex-situ* MP program started slowly in Italy, but it developed over time thanks to the good results obtained. Most Italian transplant centers currently participate in the program, and most perfused organs (60-95%, depending on the type of organ) undergo transplantation, increasing the use of organs that would otherwise have been discarded.

Conclusions. The Italian experience shows the effectiveness of using MP for organ preservation and the potential positive effect of this activity on the health care system. National data recording needs to be better structured to reinforce this evidence so that the competent authority can support transplant centers in obtaining funds or reimbursements from health care institutions.

Key words: organ preservation, solid organ transplantation, machine perfusions, normothermic, D-HOPE

Received: August 5, 2022
Accepted: September 21, 2022

Correspondence

Silvia Trapani
Italian National Transplant Center/Italian National Health Institute, via Giano della Bella 34, 00161 Rome, Italy.
Email: silvia.trapani@iss.it

How to cite this article: Trapani S, Vespasiano F, Masiero L, et al. Machine perfusion in Italy. The evolution of the clinical practice. EJT 2023;1:4-12. https://doi.org/10.57603/EJT-003

© Copyright by Pacini Editore Srl

OPEN ACCESS

This is an open access article distributed in accordance with the CC-BY-NC-ND (Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International) license. The article can be used by giving appropriate credit and mentioning the license, but only for non-commercial purposes and only in the original version. For further information: https://creativecommons.org/licenses/by-nc-nd/4.0/deed.en

INTRODUCTION

The organ shortage and the imbalance with the requests of organ waiting lists, means that the use of marginal grafts, defined according to extended criteria donors (ECD), was a valid strategy with which to enlarge the donor pool in recent years [1,2]. The use of ECD is linked to an increased risk of post-transplant complications, however, such as primary graft failure or other organ-specific dysfunction, such as late biliary injuries in liver transplantation [3-5]. Organ preservation using machine perfusion (MP) minimizes this risk, making it possible to extend the life of a retrieved graft and sometimes improving its functionality.

MP was developed in fields such as donation after death determined according to circulatory (DCD) and neurological (DBD) criteria under Extracorporeal Membrane Oxygenation (ECMO) treatment prior to death, or particular clinical situations such as organizational needs or the procurement of marginal organs [1,6].

In addition to the immediate advantage provided by MP in reducing ischemia-reperfusion damage, organ preservation must be considered as a technology that can impact the health care system, enabling a series of advantages and/or disadvantages. In a recent study, De Simone and Ghinolfi carried out a systematic review of hospital-based health technology assessments of *ex-situ* MP in adult liver transplantation. The study reported the advantages of MP in reducing the risk of early allograft dysfunction and ischemic biliary complication, potentially improving one-year graft and patient survival, and the graft discard rate [7]. Similar studies on lung and kidney transplantation showed the same results [8,9]. This approach would positively affect hospital stays and costs if MP was less expensive. Only two studies have specifically addressed this subject, with very different per-patient costs from country to country, depending on the policies of health providers [10,11]. It is for these reasons that centers continue to have difficulties using MP.

In 2017, in order to support the use of ECD and organ preservation by transplant centers, the Italian National Transplant Center "(Centro Nazionale Trapianti, CNT)" issued a national reference document for the management of organ donation supporting and guiding transplant centers in using grafts from DCD and extended criteria DBD donors. Recommendations in favor of the extended use of *in-situ* normothermic regional perfusion in DCD donors, followed by *ex-situ* MP after organ recovery, were based on the high risk of ischemic damage due to the mandatory 20 minute stand-off for legal death certification. A national organ perfusion protocol ensuring the systematic data collection of all MP procedures in the country intended to assess the effectiveness and efficiency of the method was also approved in the same year [12,13].

This study evaluated the evolution of organ perfusion activity in Italy, the effect on the transplantable organ pool, and the quality of results. It also made a preliminary evaluation of the suitability of organ *ex-situ* machine perfusion.

MATERIALS AND METHODS

The "Methods of organ perfusion in transplantation" was adopted in 2017, including recommendations for implementing a national program. A database was set up in order to collect the data for *ex-situ* perfused organs, procured from DCD or DBD donors after regional *in-situ* perfusion with the following main aims: 1) obtaining systematic information and data as a reference for the national, regional and hospital-based health technology assessment (HTA) of MP procedures; 2) offering the transplant network updated results regarding DCD and DBD discarded or utilized *ex-situ* perfused organs; 3) collecting early transplant outcomes at 1-3 months; 4) facilitating homogeneous and comparable clinical criteria and timings for the use of MP in Italian transplant centers; and 4) reporting any complication or adverse event related to *ex-situ* MP. Data was provided by transplant centers and activity results were periodically summarized in a newsletter shared with the entire donation and transplantation national community.

Some simple preliminary indications were proposed: the use of MP was recommended in DCD and extended criteria DBD kidneys, with attention to functional perfusion parameters; the use of MP was strongly suggested in liver transplantation, especially in the case of DCD grafts; and *ex-vivo* lung perfusion (EVLP) was considered necessary for lung transplants from DCD donors. Specific recommendations were also produced regarding the allocation and consent of potential recipients. In Italy, the use of MP in heart transplantation is still restricted to DBD grafts, and to a small number of centers: no specific recommendations were set in this case, since no heart procurement program from DCD donors is presently active.

The present study analyzed data for *ex-situ* organ perfusion and related transplants. The percentage of discarded organs after MP was calculated. One year recipient and graft survival was registered in the CNT Informative Transplant System (SIT) database and linked to each MP. The outcomes of all the DBD and DCD transplants performed in a specific time interval in Italy were considered to compare survival rates.

MP procedures performed in Italy were updated based on a survey carried out by transplant centers in 2022. A questionnaire was sent to all transplant centers (38 kidney, 22 liver, 10 lungs, and 16 heart). All 86 centers answered.

The effect of using MP on the pool of organs available for transplantation was evaluated by comparing the number of perfusions performed by centers with MP to the total number of organ transplants that they performed.

Statistical analysis

Descriptive statistics included the total number and percentage for categorical variables. As several continuous covariates showed a skewed distribution, median and interquartile range (IQR) were used as summary statistics. Associations between categorical variables were evaluated by chi-square test; Fisher's exact test was preferred for sparse tables. The outcomes in the survival analysis were the graft survival, defined as the time from

transplant to either graft failure or patient death, whichever occurred first. The Kaplan-Meier estimator was used to estimate the post-transplant graft survival probability. 95% confidence intervals are reported, along with the point estimations. The log-rank test was used to compare groups. Factors with p-values of < 0.05 were considered as independently predictive of the outcome. All analyses were performed using Stata version 17.0 StatCorp LLC Texas USA.

RESULTS

Questionnaire results

Sixty-two percent of the transplant centers performed at least one MP procedure (53/86) up to 2020. Eight percent more centers started using MP in 2021.

Detailed data for MP availability, number of procedures performed, including methods and final decisions about organ suitability, were collected from a total of 53 transplant centers; 15 liver (since 2015), out of the total 22; 26 kidney (since 2017) out of the total 38; 9 lung (since 2011), out of the total 10; and 3 heart (since 2017) out of the total 16. 1615 MP procedures were undertaken in nine years (2011-2020).

There were 12,027 organ transplants performed in total by the centers using MP (50.4% liver, 36% kidney, 10.7% lung and 2.9% heart) compared to 16,739 transplants performed by all centers (43.4% liver, 42.9% kidney, 7.8% lung and 5.9% heart) (Tabs. I-IV).

Liver transplantation

From 2015 to 2020, 336 liver grafts (LGs) from DBD were perfused and 322 (95.8%) were also transplanted, which is equal to 5% of 5,905 liver transplants (LTx) performed in the period by the centers using MPs. We observed an important increase in the number of LTx performed with perfused grafts over time, from 0.3% in 2015 to 12% of the total LTx performed in 2020. We observed the same trend in liver perfused grafts from DCD (Fig. 1). Of the overall DBD and DCD transplant activity, 487 out of 6,070 LTx performed were perfused grafts, equal to 8% of total LTx performed by the centers using MP, and with an increasing trend from 1% in 2015 to 16% in 2020 (Tab. I). Finally, only three liver transplant centers (LTCs) carried out this activity in 2015; in 2020, 17 out of the total 22 LTCs performed *ex-situ* organ perfusion.

No significant differences were observed in one-year graft survival between DBD and DCD perfused grafts (one-year graft survival being 90.6% [95% CI (86.0-93.7)] and 89.8% [95% CI (83.4-93.8)] respectively, p = 0.87), or between perfused grafts (DBD+DCD) and non-perfused grafts (one-year graft survival being 90.3% [95% CI (86,8-93.0)] *vs* 88.1% [95% CI (87.3-88.9)] respectively, p = 0.49), and

Table I. Liver transplants (LTx) performed with perfused grafts in 15 centers (LTCs) with MP facilities *vs* total transplants performed in Italy.

	Total LTx performed in the year	LTx performed in LTCs with MP facilities	Total of LTx from DCD + DBD perfused grafts	% LTx from perfused grafts/LTx performed in LTCs with MP facilities
2015	1071	925	7	1%
2016	1214	1007	40	4%
2017	1295	1075	46	4%
2018	1220	1016	86	8%
2019	1277	1062	150	14%
2020	1182	985	158	16%
	7259	6070	487	8%

Table II. Kidney transplants (KTx) performed with perfused grafts in 26 centers (KTCs) with MP facilities *vs* total kidney transplants in Italy.

	Total KTx performed in the year	KTx performed in KTCs with MP facilities	Total of KTx from DBD perfused grafts	Total of KTx from DCD perfused grafts	Total of KTx from DCD + DBD perfused grafts	% KTx from perfused grafts/KTx performed in KTCs with MP facilities
2017	1935	1031	72	38	110	11%
2018	1828	1145	150	56	206	18%
2019	1799	1127	138	84	222	20%
2020	1623	1022	128	64	192	19%
	7185	4325	488	242	730	17%

Table III. Lung transplants (LungTx) performed with perfused grafts in 15 centers (LungTCs) with MP facilities *vs* total transplants performed in Italy.

	Total LungTx performed in the year	LungTx performed in LungTCs with MP facilities	DBD graft LungTx	DCD graft LungTx	Total of LungTx from DBD perfused grafts	Total of LungTx from DCD + DBD perfused grafts	% LungTx from perfused grafts/LungTx performed in LungTCs with MP facilities
2011	120	117	117		6	6	5%
2012	113	109	109		12	12	11%
2013	141	135	135		11	11	8%
2014	126	123	122	1	17	18	15%
2015	112	111	110	1	11	12	11%
2016	147	143	143	0	11	11	8%
2017	144	143	140	3	14	17	12%
2018	143	140	137	3	11	14	10%
2019	153	152	139	13	13	26	17%
2020	115	113	110	3	3	6	5%
	1314	1286	1262	24	109	133	10%

Table IV. Heart transplants (HTx) performed with perfused grafts in 3 centers (HTCs) with MP facilities *vs* total transplants performed in Italy.

	Total HTx performed in the year	HTx performed in HTCs with MP facilities	Total of HTx from perfused grafts	% HTx from perfused grafts HTx performed in HTCs with MP facilities
2017	265	96	14	15%
2018	232	85	19	22%
2019	246	84	7	8%
2020	238	81	7	9%
	981	346	47	14%

between perfused and not perfused DBD grafts (one-year graft survival being 90.6% [95% CI (85.9-93.7)] *vs* 88.1% [95% CI (87.3-88.1) respectively, p = 0.67, Fig. 2A].

Kidney transplantation

Between 2017 and 2020, 528 DBD kidney grafts (KGs) were perfused and 488 (92%) were also transplanted, equal to 11.3% of 4,325 kidney transplants (KTx) performed in the period by the centers using MP (26/38). In the same period, 328 DCD kidneys were perfused and 242 (73%) were transplanted (Fig. 3). Out of 856 (DBD+DCD) perfused kidney grafts, 730 were transplanted in these centers, which is equal to 17% of overall KTx performed by the same centers (Tab. II).
In 2017, only 16 out of 42 kidney transplant centers (KTCs) carried out this activity, rising to 26 in 2020. No clinically significant differences were observed in one-year graft survival between DBD and DCD perfused grafts (one-year graft survival being 99.2% [95% CI (97.6-99.7)] and 96.3% [95% CI (92.7-99.1)] respectively, p = 0.28), and between perfused grafts (DBD+DCD) and non-perfused grafts (one-year graft survival being 97.4% [95% CI (97.2-97.6)] *vs* 98.1% [95% CI (96.7-99.0)] respectively, p = n.d., and between perfused and non-perfused DBD grafts (one-year graft survival being 97.4% [95% CI (97.2-97.6)] *vs* 99.2% [95% CI (97.6-99.7) respectively, p = n.d., Figure 2B].

Lung transplantation

Italian lung transplant centers started performing EVLP in 2011 in DBD and in 2014 in DCD, with 218 procedures overall (173 from DBD and 45 from DCD), and 137 (62.8%) transplants performed, 113 (65.3%) from DBD and 24 (53.3%) from DCD, respectively. Compared to the liver, the number of performed perfusions did not increase steadily, but there were irregular peaks over the years. (Fig. 4). Initially, there were only four lung transplant centers that adopted EVLP (out of 10 overall centers), and to date all centers can use EVLP.
With respect to the overall DBD transplant activity, the

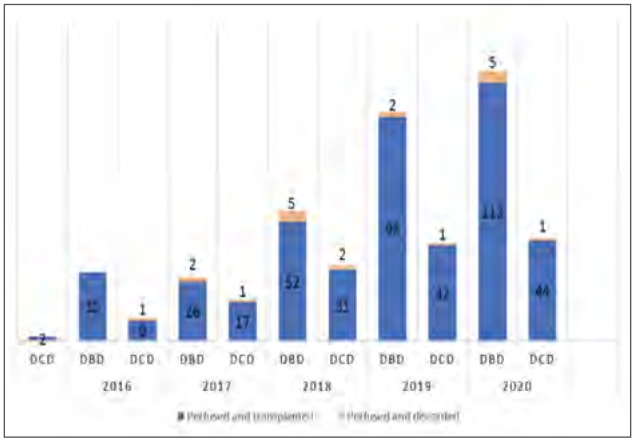

Figure 1. Liver grafts perfused and transplanted.

percentage of lungs transplanted after EVLP was 8.9% (113/1263), and if we consider total transplants (DBD + DCD) performed by the centers using MP, the percentage of lungs transplanted after EVLP increases to 10.6% (137/1287; Table III), despite of the important setback observed during the COVID-19 pandemic.

No statistically significant difference in transplant outcome was observed when comparing perfused grafts (DBD+DCD) and non-perfused grafts, with one-year graft survival at 90.4% [95% CI (84-94.3)] *vs* 93% [95% CI (91.7-94), p = 0.15] respectively.

The one-year graft survival of DBD perfused grafts was 89% [95% CI (82-94)], which is lower than that of non-perfused DBD grafts (93% [95% CI (92-94), p = 0.6), but the difference was not statistically significant (Fig. 2C).

Heart transplantation

Between 2017 and 2020, 56 heart grafts (HGs) from DBD were perfused in only 3 out of 16 heart transplant centers (HTCs), and 47 of them (84%) were transplanted, corresponding to 4.8% of 982 heart transplants performed in the period by the centers using MP. The annual trend of perfused and transplanted hearts shows an important decrease in MP activity (-52%) from 2018 to 2020 (Fig. 5). The activity of the three centers compared to their transplant activity demonstrates a corresponding decrease from 2018 (22%) to 2020 (9%), as shown in Table I.

One-year overall graft survival was lower for non-perfused grafts compared with perfused grafts, although the difference was not statistically significant (one-year graft survival being 93.0% [95% CI (92.0-93.0)] *vs* 97.0% [95% CI (81.0-100)] respectively, p = 0.12).

Although the current use of *ex-vivo* heart perfusion (EVHP) is limited to three HTCs, participation will probably increase in the near future because a further three Italian centers already have MP available, and four more will acquire it shortly.

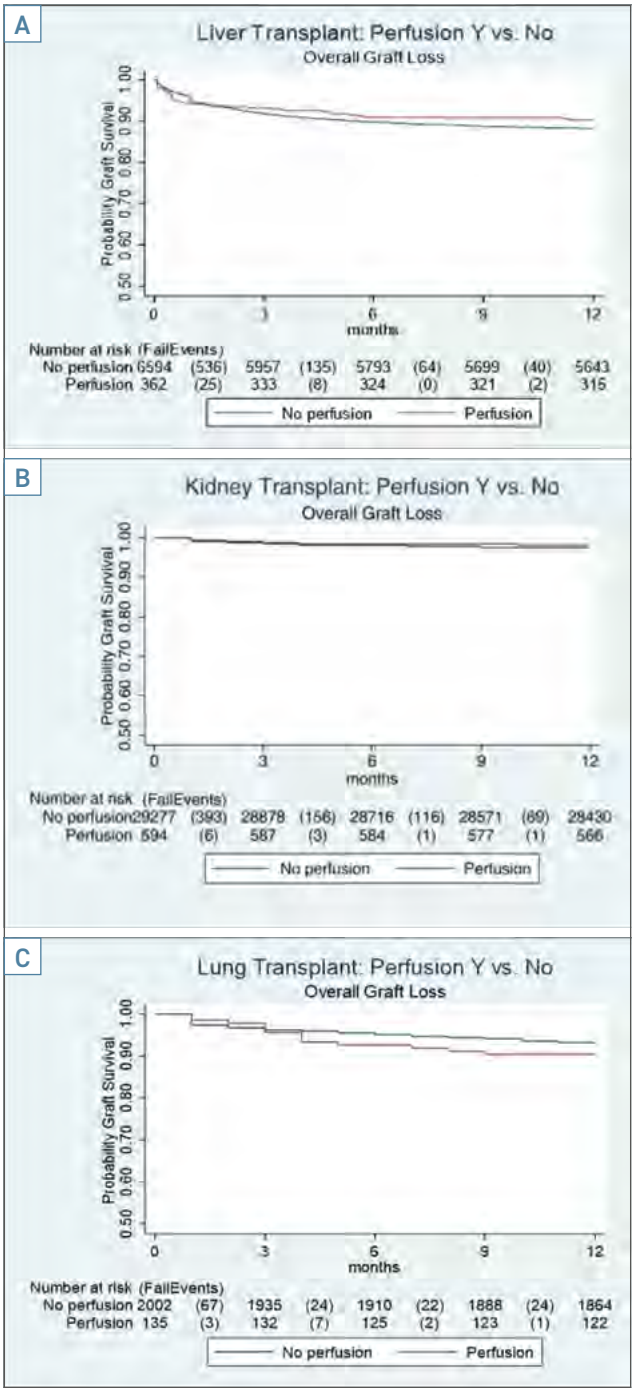

Figure 2. A) liver graft survival; B) kidney graft survival; C) lung grafts survival.

DISCUSSION

The use of ECD, including DCD and marginal DBD, is a feasible solution to organ shortage and long waiting lists. The *ex-situ* perfusion of ECD organs is one of the most promising procedures offered to the transplantation community in recent years.

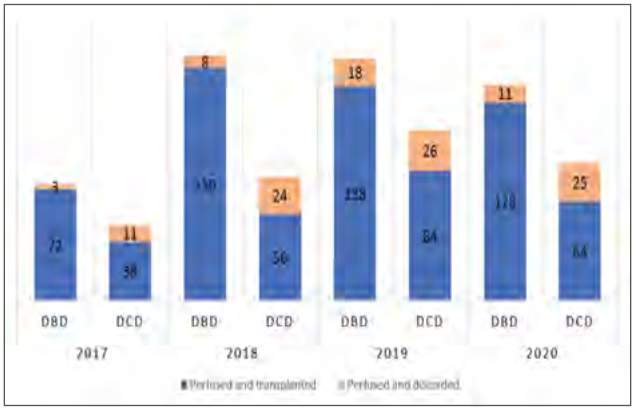

Figure 3. Kidney grafts perfused and transplanted.

Figure 5. Heart grafts perfused and transplanted from DBD.

The use of normothermic *ex-situ* MP has potential advantages, such as the ability to observe and measure organ biochemical performance and quality during the preservation period, while hypothermic perfusion decreases cellular metabolism requirements and reduces potential reperfusion-ischemic damage; in both cases, MP can also help to extend the time to complete pending organ suitability investigations at the time of organ procurement, improving transplant safety [7-9,14-19]. The ability to preserve an organ for longer also helps in solving eventual logistical-organizational problems, such as the unavailability of a theatre, surgical/anesthesiology team, or a bed in intensive care, which would prevent the transplant center being able to accept the organ and perform the transplant [11,15]. This allows the donation resource to be used in the best possible way, reducing the percentage of discarded organs and improving the performance of the system.

Italian national data is currently relatively heterogeneous, but MP may be efficient in expanding the pool of available organs and increasing the number of transplants. The crude numbers certainly suggest that organ preservation in Italy began slowly, with the recommendations set up by CNT, and gradually developed based on the good results obtained.

Certainly, the costs of the MP procedure has been one

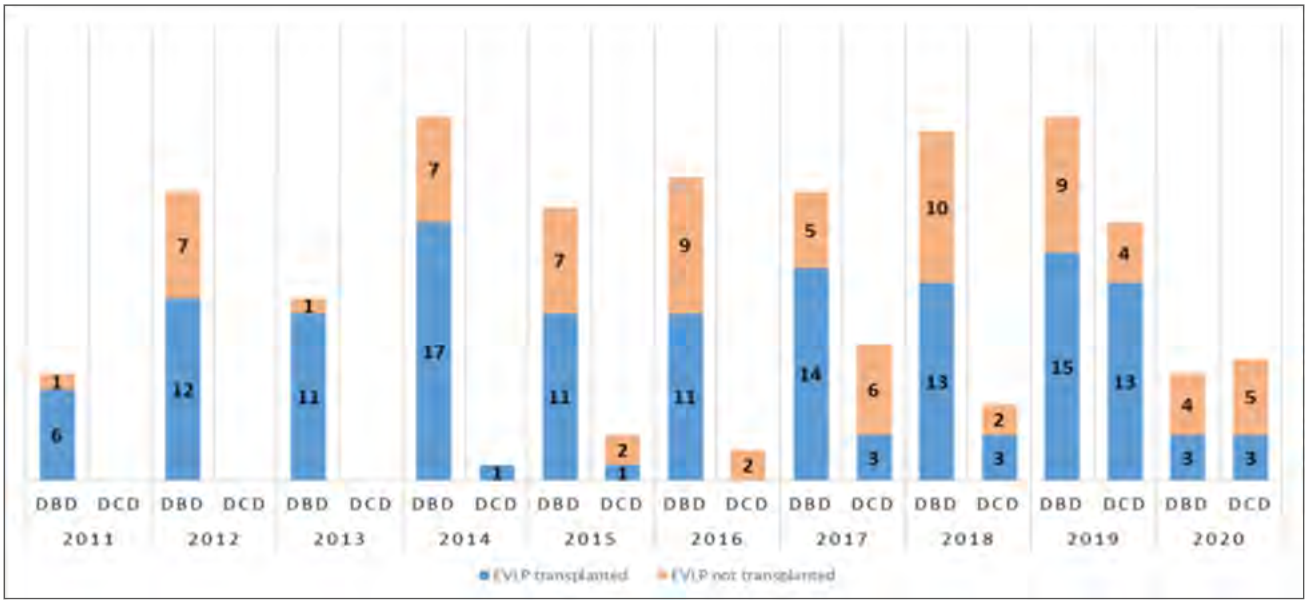

Figure 4. EVLP procedures transplanted *vs* not transplanted in the period.

of the most limiting factors in the development of the program: transplant hospitals struggle to find suitable financial resources to support the activity, especially now that it has changed from an initial experimental period to a more stable phase. Most of the high-volume transplant centers now have a MP program. Furthermore, both the consolidated results, as well as the growth of evidence-based scientific knowledge in this field, should allow the structured use of MP over time. Although a shared agreement has not yet been reached regarding indications for the use of MP, most Italian transplant centers are working in this direction, under the CNT supervision.

The role of the CNT as the competent authority for the donation and transplantation field, is to support and guide innovative procedures that can have a positive effect on transplant activity in terms of increasing the number of transplants and improving the entire donation and transplantation process.

CNT established the systematic collection of national perfusion data in order to support MP activity, promote its development over time and collect measurable indicators of effectiveness, such as the expansion of the organs pool available for transplantation. This is essential so as to measure the effectiveness of the program and to demonstrate the strategic relevance of the results, in order to encourage health authorities to support the program.

The present study has demonstrated a remarkable increase in *ex-situ* perfusion procedures, with a gradual implementation of MP in Italian kidney, liver, and lung transplant centers, up to around 10% for those centers participating in the program. Although comparisons between the outcomes of *ex-vivo* perfused and not-perfused organs are limited by the lack of detailed clinical data, and by potential differences in MP criteria among the centers, and across the years, the one-year graft survival rates of perfused grafts are very satisfactory, from both DBD and DCD donors, and they are similar to those of non-perfused DBD organs. The results demonstrate that the outcomes of perfused grafts are more than acceptable for liver, lung and kidney transplants, encouraging the transplant community to implement MP facilities and increase the use of MP.

Our analysis has some limitations: an important limitation is related to the small number of DCD donors considered, and, most of all, to the inclusion of both controlled and uncontrolled DCD together in the data analysis. Only one-year graft survival rates were studied, in the absence of complete information on complications, duration of hospital stay and long-lasting follow-up.

Lastly, it is not clear whether the increase in the organ pool is the only effect of MP utilization or if other variables may have played a role over the period. Although some of the evidence in our analysis is very promising, there is a clear need for more information from high quality and appropriately powered trials.

More generally, the standardization of data collection and reporting will allow comparisons of trials [20]. The standardization of nomenclature for MP in order to maximize consistency and to enable reliable comparisons and meta-analyses of studies is a fundamental and urgent prerequisite for national and international comparisons of results [21].

Conflicts of interest and the relationships between researchers and commercial medical industry is a critical issue. The role of external (particularly commercial) parties in trial design and analysis should be clearly stated, including that of the holders of data and the parties responsible for analysis, as these relationships have the potential to affect study validity and interpretation [20].

Most published studies have been funded by private companies, and are thus potentially biased due to commercial reasons/interests. Multicenter studies in the MP field are urgently needed, and the national transplant authorities could thus be the ideal reference point for reliable data, free from any professional or economic conflicts of interest.

Information about the cost of MP is not easily available, and cost-benefit analysis needs reliable clinical and organizational data, as well as prolonged follow-up for transplant recipients and their quality of life.

Strategies to counterbalance the increased costs of organ transplantation are needed from the perspective of the Italian national health system-based hospital practice and disease-related group reimbursement policy [7]. These strategies should be developed and tested at regional and national level. Ad hoc education and adequate medical and technical personnel resources should be programmed; the standardization of procedures and transparency of clinical results should be guaranteed, particularly when marginal organs are used and offered for consent to patients on the waiting list. The national transplant network and patients could both take advantage of the clear periodical CNT website publication of MP results and recipient follow-up.

The effectiveness and suitability of transplanted patient treatments are critical issues in the clinical governance of the national network. In Italy, the CNT is responsible for the suitability and safety of novel technical procedures included in the clinical management in the centers. Specifically, innovative procedures based on artificial treatments of organs after retrieval for function evaluation and final decision of usability should be evaluated and eventually approved by CNT.

A national consensus committee is thus desirable, to address the clinical and organizational criteria for *ex-situ* organ perfusion, functional evaluation and organ usability in the different donation pathways (DBD, uncontrolled and controlled DCD) and context (e-CPR prior-to-death, transportation, and delayed allocation). Clinical criteria

should be revised annually: nationally collected data on transplant outcome and complications, possible adverse events related to MP, cost benefit analysis, new procedures and published multicenter study.
A clear methodology and shared responsibility should be ensured in data collections from transplant centers and regional transplant centers towards the CNT Informative Transplant System (SIT). All perfused organs should be included in the ad hoc national MP dataset and related outcomes in the quality database. Each center could take advantage of the complete reliable data and compare local results with national results, or develop proper single center or multicenter research projects.
Adequate datasets should be defined for national and local registries to enable reliable health technology assessment, including clinical indications, cost-effectiveness, economical sustainability, and criteria for the diffuse implementation of innovative procedures as the *ex-situ* graft MP.
Each region should include MP in its annual program and planning document, and consider the number of cases for each organ transplant program, personnel support and quality clinical data collection aim at proper technology assessment, funding for machine availability, external technical support, and disposable materials. A dedicated personnel educational pathway should be designed on the basis of nationally validated standards.
Public-private cooperation could be considered if clear rules are respected, and activities are independently monitored. Facilitating models for public-private collaborative research in this field are desirable.
Different operative modalities for machine availability may be considered and tested, including service, leasing, and purchase with shared regional or national public procurement systems. Any adverse event or complication related to *ex-situ* MP should be immediately reported to the CNT and regional transplant coordinator, and audited.
The national expert committee chaired by CNT, should analyze clinical results annually, and approve procedures or suggest corrective actions.

CONCLUSIONS

Ex-situ organ perfusion may now be a way to expand the pool of organs available for transplantation. MP effectiveness is supported by well-established clinical evidence, but this still lacks clear shared indications. It is necessary to implement this activity as far as possible in order to consolidate the scientific evidence and increase the number of centers that use MP. Machine perfusion technology and innovative clinical procedures are thus a strategic target for the Italian transplant network and the national transplant authority (CNT).
The CNT can help centers to reduce the cost of MP, which is the main obstacle to their implementation in all transplant centers.
A solid and well-structured national data collection is the only way to obtain the clinical evidence of results and efficacy that could allow dedicated funds or ad hoc reimbursement to be received for this activity, such as DRGs. Over the time, this activity could become cost-effective and affordable, because increasing perfusions means we could obtain a reduction in the price of MP facilities and more transplants at lower cost. The use of MO could also have a positive effect on complications after transplants, reducing patient hospital stays, and thus a highly positive effect on overall health care system.

Acknowledgements

We wish to thank all the transplant centers of the Italian National Transplant Network who collaborated with us to collect these data.

Conflict of interest statement

The Authors declare no conflict of interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contributions

ST: designed the work, analyzed and interpreted data, drafted the work, approved the final version and reviewed the accuracy and integrity of the work; FV: designed the work, methodology, data management, approved the final version; FP: designed the work, analyzed and interpreted data, revisited critically the manuscript for intellectual content, approved the final version and reviewed the accuracy and integrity of the work; MC: designed the work, analyzed and interpreted data, revisited critically the manuscript for intellectual content, approved the final version and reviewed the accuracy and integrity of the work; FP: methodology, data management, supervision, approved the final version; LM: methodology, data management and statistical analysis, approved the final version; ST: methodology, data management and statistical analysis, approved the final version; PF: acquisition and interpretation of data, writing, approved the final version; DP: acquisition and interpretation of data, writing, approved the final version; AO: acquisition and interpretation of data, writing, approved the final version.

Ethical consideration

Not applicable.

References

1 Vodkin I, Kuo A. Extended criteria donors in liver transplantation. Clin Liver Dis 2017;21:289-301. https://doi.org/10.1016/j.cld.2016.12.004

2 Chaney J, Suzuki Y, Cantu E 3rd, et al. Lung donor selection criteria. J Thorac Dis 2014;6:1032-1038. https://doi.org/10.3978/j.issn.2072-1439.2014.03.24

3 Sousa Da Silva RX, Weber A, Dutkowski P, et al. Machine perfusion in liver transplantation. Hepatology 2022;Apr 30. https://doi.org/10.1002/hep.32546 [Epub Ahead of Print]

4 Bifulco O, Bottio T, Caraffa R, et al. Marginal versus standard donors in heart transplantation: proper selection means heart transplant benefit. J Clin Med 2022;11:2665. https://doi.org/10.3390/jcm11092665

5 Cypel M, Yeung JC, Liu M, et al. Normothermic ex-vivo lung perfusion in clinical lung transplantation. N Engl J Med 2011;364:1431-1440. https://doi.org/10.1056/NEJMoa1014597

6 Van Raemdonck D, Neyrinck A, Cypel M, et al. Ex-vivo lung perfusion. Transpl Int 2015;28:643-656. https://doi.org/10.1111/tri.12317

7 De Simone P, Ghinolfi D. Hospital-based health technology assessment of machine perfusion systems for human liver transplantation. Transpl Int 2022;35:10405. https://doi.org/10.3389/ti.2022.10405

8 McMeekin N, Chrysos AE, Vale L, et al. Incorporating ex-vivo lung perfusion into the UK adult lung transplant service: an economic evaluation and decision analytic model. BMC Health Serv Res 2019;19:326. https://doi.org/10.1186/s12913-019-4154-6

9 Tingle SJ, Figueiredo RS, Moir JA, et al. Machine perfusion preservation versus static cold storage for deceased donor kidney transplantation. Cochrane Database Syst Rev 2019;3:CD011671. https://doi.org/10.1002/14651858.CD011671.pub2

10 Webb AN, Lester ELW, Shapiro AMJ, et al. Cost-utility analysis of normothermic machine perfusion compared to static cold storage in liver transplantation in the Canadian setting. Am J Transplant 2022;22:541-551. https://doi.org/10.1111/ajt.16797

11 Javanbakht M, Mashayekhi A, Trevor M, et al. Cost-utility analysis of normothermic liver perfusion with the OrganOx metra compared to static cold storage in the United Kingdom. J Med Econ 2020;23:1284-1292. https://doi.org/10.1080/13696998.2020.1804391

12 Italian National Transplant Center (https://www.trapianti.salute.gov.it/imgs/C_17_cntPubblicazioni_25_allegato.pdf, accessed July 21, 2022).

13 Italian National Transplant Center (https://www.trapianti.salute.gov.it/trapianti/archivioProtocolliCnt.jsp?lingua=italiano&anno=2016&btnCerca=cerca, accessed July 21, 2022).

14 Serifis N, Matheson R, Cloonan D, et al. Machine perfusion of the liver: a review of clinical trials. Front Surg 2021;8:625394. https://doi.org/10.3389/fsurg.2021.625394

15 Brüggenwirth IMA, Mueller M, Lantinga VA, et al. Prolonged preservation by hypothermic machine perfusion facilitates logistics in liver transplantation: a European observational cohort study. Am J Transplant 2022;22:1842-1851. https://doi.org/10.1111/ajt.17037

16 Elliott TR, Nicholson ML, Hosgood SA. Normothermic kidney perfusion: an overview of protocols and strategies. Am J Transplant 2021;21:1382-1390. https://doi.org/10.1111/ajt.16307

17 De Carlis R, Lauterio A, Centonze L, et al. Italian DCD Collaborator Group. Current practice of normothermic regional perfusion and machine perfusion in donation after circulatory death liver transplants in Italy. Updates Surg 2022;74:501-510. https://doi.org/10.1007/s13304-022-01259-9

18 Hessheimer AJ, Gastaca M, Miñambres E, et al. representation of the SETH Working Group on DCD. Donation after circulatory death liver transplantation: consensus statements from the Spanish Liver Transplantation Society. Transpl Int 2020;33:902-916. https://doi.org/10.1111/tri.13619

19 O'Neill S, Srinivasa S, Callaghan CJ, et al. Novel organ perfusion and preservation strategies in transplantation – where are we going in the United Kingdom? Transplantation 2020;104:1813-1824. https://doi.org/10.1097/TP.0000000000003106

20 Patrono D, Cussa D, Rigo F, et al.; Liver Machine Perfusion Survey Group. Heterogeneous indications and the need for viability assessment: an international survey on the use of machine perfusion in liver transplantation. Artif Organs 2022;46:296-305. https://doi.org/10.1111/aor.14061

21 Martins PN, Rizzari MD, Ghinolfi D, et al. ILTS Special Interest Group "DCD, Preservation and Machine Perfusion". Design, analysis, and pitfalls of clinical trials using ex-situ liver machine perfusion: the International Liver Transplantation Society Consensus guidelines. Transplantation 2021;105:796-815. https://doi.org/10.1097/TP.0000000000003573

22 Karangwa SA, Dutkowski P, Fontes P, et al. Machine perfusion of donor livers for transplantation: a proposal for Standardized Nomenclature and Reporting Guidelines. Am J Transplant 2016;16:2932-2942. https://doi.org/10.1111/ajt.13843