




## ORIGINAL ARTICLE

# Comparing demographics of organ donor referrals from the intensive care unit and outside units

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## SUMMARY

The Spanish organ donation system is a world leader in organ recovery. One of Spain's strategies is the identification of organ donor referrals outside of the intensive care unit (ICU) for intensive care to facilitate organ donation (ICOD). There are limited data comparing the profiles of ICU-based and non-ICU ICOD referrals. This single-center retrospective chart review analyzed organ donor referrals of ICU and non-ICU patients to better understand the demographic and clinical differences between cohorts. The primary outcome was to understand if organ donation conversion rates were similar between ICU and non-ICU referrals. We collected data from 745 organ donor referral candidates, 235 (32%) of whom entered ICOD protocols. Out of this cohort, 144 (61%) became actual organ donors, 37 of whom (26%) were referred from non-ICU units. The ICU had the highest organ donor conversion rate (66% of ICU ICOD patients became actual organ donors) whereas non-ICU referrals had a 51% conversion rate. Non-ICU unit donors contributed to 21% and 26% of all kidney and liver donations, respectively. Though organ referral candidates from non-ICU units contribute to a small proportion of actual donors, their donated organs are important to sustaining organ donation and transplant activity.

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## Key words

critical care, emergency service, hospital, tissue and organ recovery

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## Introduction

The Spanish organ donation and transplant system is recognized internationally, with 48.3 donors per million and 114 transplants performed in 2018 [1]. The success of Spain's organ donation system is attributed to three main factors: broadening criteria for organ donation, creating protocols to promote organ donation after circulatory death, and identifying possible organ donors outside of the intensive care unit (ICU) setting to

incorporate organ donation into end-of-life protocols for all eligible patients [2]. Intensive care to facilitate organ donation (ICOD) has been implemented in recent years to include organ donation into end-of-life care for eligible patients in and outside the ICU. ICOD is defined as the initiation or continuation of intensive care practices like elective non-therapeutic ventilation, and hemodynamic support for patients in whom therapeutic treatment has been deemed futile. ICOD allows these patients to evolve to brain death in a controlled

setting so that they have the opportunity to donate their organs [3,4].

Still, several studies have shown that many possible organ donors pass through the emergency department (ED), die outside of the ICU, and are never considered as possible organ donors [4–7]. In 2016, the Spanish Organización Nacional de Trasplantes (ONT) collaborated with the Spanish Society of Emergency Medicine to increase identification of possible organ in the ED [5]. These guidelines advocate for early identification of possible donors by implementing formalized training for ED physicians and staff to increase understanding of the organ donation process and the criteria used to evaluate possible donors [5]. Recent efforts in Spain have focused on training physicians in other units like the Stroke Unit and general hospital wards to also understand the organ donation process and identify potential organ donors on their medical services [8,9]. The efficacy of this effort and potential for non-ICU-admitted patients to convert to organ donors is poorly characterized. We hypothesized that patient donor referrals from units outside the ICU like the ED, Stroke Unit, and other wards will have similar organ donation conversion rates to patients referred from the ICU.

## Patients and methods

### Relevant definitions

#### *Referral candidate*

A patient with a devastating brain injury who is being clinically treated for their injury and is referred to the organ transplant coordinator team for clinical monitoring.

#### *Possible donor*

A patient with devastating brain injury in whom curative treatment has been deemed futile and organ donation is being considered to incorporate into end-of-life care [10].

#### *Actual organ donor*

A patient who has died and has undergone a surgical operation to donate individual organs [10].

#### *Utilized organ donor*

A patient who has died and has had an organ or organs donated and transplanted to another person [10].

We performed a retrospective database review of patients defined as organ donor referral candidates from January 2013 to February 2019 at the Miguel Servet University Hospital in Zaragoza, Spain. The Miguel Servet University Hospital is a tertiary care referral hospital for the autonomous region of Aragon with 1213 inpatient beds [11]. The hospital has trauma, neurosurgical, critical care, and transplant surgery teams among its medical services [11]. The hospital is recognized as a specialized stroke center by the European Union and cares for many patients with devastating neurologic injuries [12]. There are 4 ICUs (trauma, polytrauma, coronary ICU, postoperative cardiac) in the hospital, with a total of 46 beds among the four units [13]. Additionally, the hospital also has a five-bed Stroke Unit for patients with neurovascular injuries [14]. This hospital serves approximately 400 000 citizens in Zaragoza and the surrounding region of Aragon [11]. Of note, this hospital donation data included the following: kidneys, livers, hearts, pancreas, and intestines, though this hospital also participated in bone and cornea donation. Each patient assessment was made on an individual basis to decide what organs could be recovered based on biopsy results, organ function, and contraindications. Though donation after circulatory death has become a prominent fixture in Spanish organ donation, this hospital only had brain death organ recovery protocols at the time of this study [15].

We identified referral candidates from the organ donor alert database, maintained by the hospitals' organ transplant coordinators, and performed a structured review for pertinent variables from the electronic medical record for all candidates. Referral candidate alerts were activated by referring physicians from multiple dispositions. These individuals were trained to alert the hospital's organ transplant coordinators when a patient under their care was diagnosed with a "potentially devastating brain injury." These injuries were defined as neurologic injuries that could lead to brain death if therapeutic treatment was not effective. At this stage, patients were identified so that they could be followed by the organ transplant coordinator peripherally. Once a patient's medical condition worsened, an interdisciplinary team including neurologists, neurosurgeons, intensivists, ward-based physicians, and emergency medicine physicians, excluding the organ transplant coordinator, conducted an evaluation to determine the patient's prognosis and indication for further clinical or surgical treatment based on the patient's current clinical status.

Once patients' futility was determined by the interdisciplinary team, the hospital's organ transplant coordinators performed their own evaluation to assess any potential contraindications to organ donation. Following that evaluation, the organ transplant coordinator conducted an interview with the patient's family members to explain the patient's clinical prognosis and to obtain the family's consent to begin ICOD protocols. If the family agreed, the patient was transferred to the ICU for ICOD protocols if they were being referred from an outside unit. If they were already in the ICU, therapeutic treatment of their medical condition was stopped and ICOD protocols were initiated. Patients were managed in accordance with ICOD protocols for a specified period decided between the organ transplant coordinator and the donor's family. If patients did not progress to brain death within the agreed-upon period, life-sustaining treatments were withdrawn. Additionally, if a patient developed contraindications to donation during ICOD protocols like multi-organ failure, or sepsis, their life-sustaining treatment was withdrawn. We labeled these cases as patients who were "not medically suitable for organ donation," as a previous study did [3]. We excluded referrals from outside hospitals to specifically focus on in-hospital donor identification. From the database, we abstracted age, gender, weight, referring unit, type of illness or injury, organs donated, and reason for not donating, if applicable.

Our primary outcome of interest was organ donor conversion rate, which was formulated by calculating the percentage of patients who became organ donors after being enrolled in ICOD protocols, stratified by referring units. We were also interested in comparing successful organ donation after referral, defined as organs that were recovered with the intent to transplant. We used descriptive statistics to summarize overall population characteristics. We compared the number of donors among referred patients, stratified by referring unit (ICU versus non-ICU), and compared the rates of organ donor conversion by using Chi Square analyses. We used STATA Version 15 (StataCorp, College Station, TX, USA) for statistical analysis. This project was given ethical approval by the Committee of Ethical Investigation of the Autonomous Region of Aragon (CEICA): C.P-C.I PI19/166 in line with the European Medicines Agency Guidelines for Good Clinical Practice.

## Results

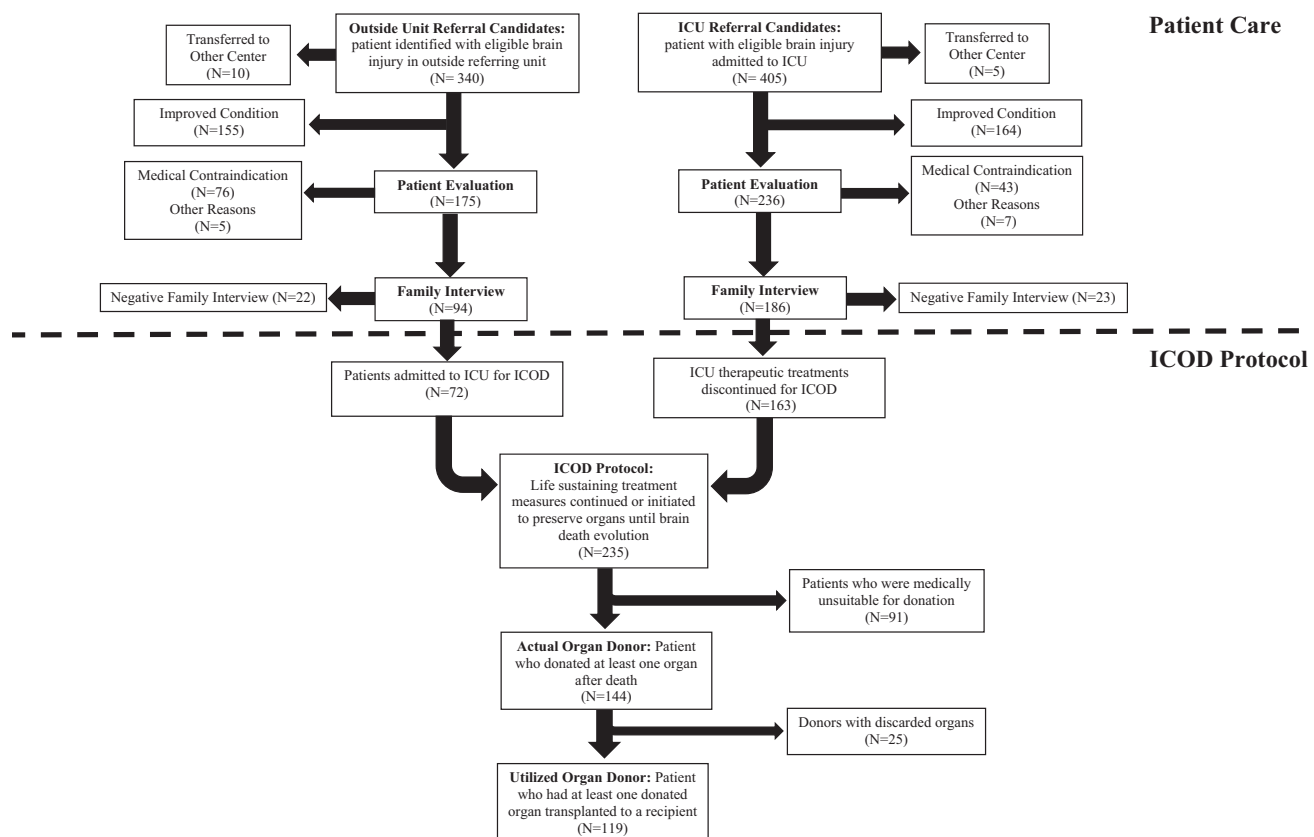
Our study examined patients who were identified with a "potentially devastating brain injury." In our study,

these cases included: anoxic brain injury, asystole, traumatic brain injury, subarachnoid hemorrhage, hemorrhagic stroke, ischemic stroke, along with other pathologies with known neurologic damage. In most cases, patients who progressed to brain death did so within 72 hours of admission which is in line with previous research [10,16,17].

Of 745 organ donation referral candidates, 405 (54%) were referred from the ICU and 340 (46%) were referred from non-ICU locations. These locations included the ED (184, 54%), Stroke Unit (138, 41%), and general hospital wards (18, 5%). Mean age was 66 + 19 years and patients referred from the ICU were significantly younger than those referred from other locations (57 +/- 19 vs. 77 +/- 11 years,  $P < 0.001$ ). Overall, 329 (45%) referrals were female and ICUs referred a significantly lower proportion of female patients (38% vs. 52%,  $P < 0.001$ ). The most common admission diagnosis was cerebrovascular pathology (546, 73%). ICUs were more likely to refer patients for organ donation after a traumatic brain injury (22%) compared to non-ICU units (13%). In contrast, non-ICU units were more likely to refer patients with cerebrovascular pathology (85%) compared to ICUs (64%).

There were many reasons organ donor referral candidates were not enrolled in ICOD protocols (Fig. 1). The most common reason patients were not enrolled was improved medical condition after therapeutic treatment (319 patients, 43% of all referrals). Many patients (119, 16%) also had medical contraindications identified during their evaluation by the organ transplant coordinator that precluded them from becoming organ donors. Of note, only 45 (16%) out of 280 patients were excluded due to family refusal for organ donation. Following ICOD protocol initiation, 91 (39%) patients were unable to donate due to unsuitable medical condition. In this group, 39 (43%) patients were identified as possible candidates for donation after circulatory death. Additionally, only 25 patients had their organs discarded after donating. Out of this cohort, 23 (92%) patients were referred from the ICU.

Of all organ donor referral candidates, 144 (19%) became actual donors, 37 of whom (26%) were referred from non-ICU units. The highest number of organ donors among the referring units was the ICU with 107 (74%) donors, followed by the ED with 26 (18%) organ donors, and the Stroke Unit with 10 (7%) donors. There was only 1 (1%) donor from other hospital units. The ICU had the highest organ donor conversion rate among referring units (Table 1). Outside units had fewer patients that were enrolled in ICOD protocols and lower conversion rates as compared to ICU patients



**Figure 1** Organ Referral Candidate Pathway. This figure annotates the specific pathways at this hospital for organ referral candidates referred from the ICU and from units outside the ICU. The dashed line indicates the transition from therapeutic patient care to enrollment in ICOD protocols with the intent to donate organs. The reasons why organ referral candidates did not progress to ICOD protocols after their initial identification are also described at each step of the pathway.

enrolled in ICOD protocols, but differences in conversion rates were not statistically significant ( $P > 0.15$ ). The average age of all organ donors was  $58 \pm 20$  years. Actual organ donors from the ICU had an average age of  $56 \pm 20$  years while the average age of actual organ donors from outside units was  $66 \pm 21$  years. There was a statistically significant difference between the organ donor cohorts' mean age ( $P < 0.01$ ).

Organ donation and transplantation occurred for patients referred from outside the ICU and those referred from inside the ICU (Table 2). On average, 3.2 organs were recovered, and 2.4 organs were transplanted on

average per actual donor. In terms of utilization, organs recovered from patients referred outside the ICU tended to have similar utilization rates compared to organs recovered from patients referred in the ICU (Table 2). Chi-square analyses comparing utilization rates between patients referred outside the ICU and those referred while in the ICU were not significant for all organs.

## Discussion

The ultimate challenge facing transplant systems across the world is the limited supply of organs in comparison to the

**Table 1.** Organ donor conversion rate by referring unit, Miguel Servet University Hospital January 2013–February 2019.

Disposition	Patients enrolled in ICOD protocols	Actual organ donors	Organ donor conversion rate (%)*
ICU	163	107	66
ED	47	26	55
Stroke unit	22	10	45
Other wards	3	1	33

\*Organ donor conversion rate = ((actual donors)/(patients enrolled in ICOD protocols))\*100.

**Table 2.** Organ donations at Miguel Servet University Hospital from January 2013–February 2019.

Disposition	Organs recovered	Organs utilized	Utilization rate*
<b>ICU</b>			
Livers	96	73	76%
Kidneys	194	146	75%
Hearts	42	21	50%
Lungs	26	22	85%
Pancreas	11	10	91%
Intestines	3	0	0%
<b>ED</b>			
Livers	24	18	75%
Kidneys	36	28	78%
Hearts	4	2	50%
Lungs	2	0	0%
Pancreas	0	0	–
Intestines	0	0	–
<b>Stroke unit</b>			
Livers	9	7	78%
Kidneys	14	10	71%
Hearts	1	0	0%
Lungs	0	0	–
Pancreas	0	0	–
Intestines	0	0	–
<b>Other wards</b>			
Livers	1	1	100%
Kidneys	2	2	100%
Hearts	0	0	–
Lungs	0	0	–
Pancreas	0	0	–
Intestines	0	0	–

Organs recovered included organs that were donated by the patients that were transplanted and those that were donated but not transplanted. Utilization rate was calculated by (organs transplanted)/(organs recovered)\*100.

\*Chi-square analyses performed to assess utilization rate by organ between units outside the ICU and the ICU were not significant.

ever-increasing demand. While much of the debate regarding improving organ recovery is based on the adoption of opt-out versus opt-in systems, recent research has shown no significant increase in the number of deceased donors in the opt-out countries [18–20]. As treatment of neurologic injuries and cerebrovascular accidents continues to improve, innovation that sustains the donor pool is urgently needed. Spain's organ recovery and transplant framework serves as a benchmark for the world for its efficiency and persistent process improvement.

The addition of ICOD protocols to patients' end-of-life care has established potential pathways for organ donation referral outside of the ICU. Recent multicenter studies from Spain also indicate that patients identified

outside of the ICU can contribute a significant amount to the possible donor pool and to each hospital's annual actual donor count [3,4,17]. These studies' findings are consistent with the results of our single-center study and emphasize the importance of identifying possible organ donors in other hospital units outside of the ICU through the ICOD pathway.

Despite the success of the ICOD pathway to increase the donor pool, there are many challenges to optimize the referral process. As seen in our study, a wide referral base was necessary to capture all the patients that had the potential to become donors during their hospitalization. This referral process requires the collaboration of physicians throughout the hospital along with the organ transplant coordinator and team. Additionally, physicians in all these referral areas must be trained and well-equipped to recognize a patient that meets the criteria for referral. This study emphasizes the complexities involved in evaluating patients for potential organ donation with an uncertain prognosis. Many of the referred patients had improved clinical conditions that allowed them to be discharged from the hospital because they had successful medical treatment for their condition. As seen in this study, a secondary effect to having broad and non-specific referral criteria is that many patients who are initially referred will not evolve to become organ donors. Future research should be directed toward creating better guidelines at identifying patients who have a high likelihood of becoming an organ donor from when they are first admitted to the hospital so that organ transplant coordinators can direct their resources and attention more efficiently. Many patients also had medical contraindications that excluded them from donation. Assessing a patient's prognosis and evolution to brain death presents its own challenges to the evaluation team. Though modern imaging techniques have helped prognosticate patients' outcomes, predicting a patient's likelihood to suffer brain death in the acute setting is difficult. Communicating this diagnosis to families presents its own challenges, and the organ transplant coordinator and treating team need to be trained to navigate these conversations appropriately.

Our data demonstrate that although ICU-admitted patients remain the primary source of referrals and actual donors, identification of possible donors in other units in the hospital is an effective strategy to expand the donor pool. Other studies have shown that though the ED is a good source of referrals and actual donors, there are still patients who are missed due to the logistical complications and fast pace of the treating environment [6,21]. Future research is needed to better understand how to prevent these referrals from being missed.

There were multiple clinical and demographic differences between ICU-admitted donors and donors from outside units. Although the non-ICU donors only made up 26% of all referrals, the donor subset yielded 21% of the total kidneys and 26% of the total livers recovered at the hospital, emphasizing the yield potential of viable organs outside the ICU. Additionally, these patients' donated organs were transplanted to recipients at a similar rate compared to patients referred from the ICU (Table 2). The age of donors from outside the ICU is an important topic that should be studied further. In several other research studies, organ donors from units outside the ICU were older than patients referred from the ICU [2,3,22]. While the average age of the organ donors from each cohort was statistically significant, the organ utilization rates of both groups were similar. This finding raises an important point that even though patients referred from outside units may be older, they are potentially more clinically stable than patients who were being treated therapeutically in the ICU prior to their referral. Additionally, patients from outside units may have had shorter lengths of hospitalization compared to patients referred from the ICU and were less likely to experience multi-organ failure and hospital-acquired infections that would preclude them from organ donation. Additional studies are needed to better understand the underlying differences between ICU and non-ICU cohorts and the effect that these differences have on donor referrals and conversion rates.

While the practice of referring organ donor patients from outside the ICU is applicable to many organ donation systems around the world, the Spanish system has several specific intricacies that enhance its performance and limit its generalizability to organ recovery systems in other countries. First, Spain has developed an extensive training program to train organ transplant coordinators at the local, regional, and national level for engaging with families prior to and during the ICOD process [2,23]. The organ transplant coordinator is typically a critical care physician or anesthesiologist that cares for patients in the ICU and manages the hospital's organ donation referral process, family interview, and organ donation logistics [24]. The coordinator's constant surveillance of referring hospital units prevents the loss of organ donor referral candidates. In our study, many patients were referred to the organ donor coordinator team for surveillance even though only a small subset evolved to become actual donors. Further, the coordinator plays an integral role in forming a relationship with the patient's family and conducting the family interview to consent to donation. In our study, only

16% of families declined organ donation; a testament to the education and support that the coordinators provide to donor's families [24]. Previous studies in Spain and other countries have illustrated the importance of the family interview in the context of the organ donation process [2,25,26]. Additionally, the organ transplant coordinators are typically compensated on an incentive-based system that helps to incentivize organ donation activity at each hospital, similar to other organ donation systems around the world [24].

The multi-level organization model of the ONT has created a formidable system of logistics and coordination to ensure that as many donors can be transplanted to recipients as possible. The ONT has played an important role in pursuing continuous improvement projects aimed at finding ways to continue to raise the country's organ donor pool [2,4,27,28]. The ONT also plays an important logistics role. Many of our hospital's actual donors' organs were donated in Zaragoza and then transported to hospitals throughout Spain to recipients if there were no available recipients in Zaragoza. The ONT is responsible for communicating with organ transplant coordinators at hospitals throughout the country to facilitate this process. The development and continued improvement of this process have allowed many donated organs to be transplanted when they would otherwise be discarded [2,29].

The implementation of controlled donation after circulatory death (cDCD) in hospitals throughout Spain has provided an alternative path for critically ill patients to donate their organs without meeting brain death criteria [15]. In our study, there were 39 patients who were identified as potential candidates for donation after circulatory death had a cDCD protocol existed at this hospital at the time of our study. Further research should be directed toward studying missed patients who could have donated their organs *via* cDCD to help advocate for the development of this donation pathway in every Spanish hospital.

Also, the Spanish system accepts possible organ donors above the age of 65 and with underlying comorbidities, who might otherwise be rejected for organ donation in other countries. This referral subsection contributes a significant amount to their total donation activity [2]. The Spanish model allocates these organs to other elderly patients even with HLA-mismatch, as has been reviewed in other European studies [30].

Finally, the ONT has focused substantial efforts to educate the public and inform them about the risks and benefits associated with organ donation. These efforts have led to increased interest and willingness to consent

to a relative's organ donation [31]. The ONT's relationship with the media to increase awareness about organ donation and to provide the public with information about the Spanish transplant system's success is crucial to its continued growth [2,26].

Our study has several major limitations. First, we had very limited clinical data available to us to extensively characterize our patients outside of the data maintained in the organ transplant coordinator database. Additional clinical data may provide demographic and clinical information to further characterize donor subsets and better understand the differences and markers that are reliable predictors of viable organ donation candidates. Additionally, we did not have available data to characterize how many patients were or were not intubated at time of referral which is important to understand the additional resources necessary to facilitate ICOD. Also, patients in this database were grouped based on their disposition at the time of their organ referral rather than their clinical status that prompted organ donation referral. Thus, it is conceivable that there were patients that had an eligible clinical status for organ donation while they were in the ED or in another unit in the hospital but were not referred for donation until they reached the ICU and vice versa. In the United States, organ donation referrals are generally grouped based on clinical status at time of referral rather than disposition in the hospital.

In conclusion, the Spanish organ donation system's strong presence in the community and in the health-care system brings together stakeholders from both

sides to allow the system to flourish. In its ability to educate the public and continually improve its organ recovery process, the Spanish organ donation system serves as a benchmark for all health systems to follow. The optimization of organ donation referral from ICUs and outside units continues to sustain the organ donor pool.

## Authorship

NK: project design, data collection, data analysis, and manuscript development. ACNP: database access and manuscript review. MPE: project design and manuscript review. JE: project design, data analysis, and manuscript review. JPM: project design, administrative approval, and manuscript review.

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## Conflict of interest

No conflicts of interest exist for any of the authors involved in this project.

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