

Cardiac Transplantation in Spain: Have We Reached Our Peak?

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Have we reached our limits in the field of heart transplantation? Can we satisfy our needs at the present rate? Are we doing our utmost to make the best possible use of our resources in this respect? Can we do more?

The answers to these questions probably vary widely depending on who voices them. The views of the transplant teams, program coordinators or the Spanish National Transplant Organization (ONT) itself do not have to be identical, mainly because the position from which each observes the process and the information to which we have access differ widely. In fact, it is more than likely that, even among cardiologists, those involved in a transplant team have a different view of the problem than those who occasionally have to evaluate a donor heart to assess its viability.

For these reasons, the report by Chamorro et al¹ that appears in this issue of *REVISTA ESPAÑOLA DE CARDIOLOGÍA*, and that gave rise to this editorial, is particularly relevant. This is a splendid opportunity to take a look at this issue, of unquestionable importance since we are dealing with a vital treatment that does not reach all the patients who could benefit from it. Thus, any chance for analysis and/or improvement should be welcome.

To begin with, a few figures that invite reflection: at this writing, we are summing up the data on donation and transplantation corresponding to 2005.² Fortunately, donation in Spain continues to grow and, once again, all the records have been broken: more than 1500 donors (3 times more than in 1989, when the ONT was created), over 35 donors per million population (we should recall that in England, Germany, or Sweden this figure is around 12 or 13), and the increases in the performance of transplantations of kidney, liver, pancreas, lung, and intestine are more than significant, with record numbers

in all of them...with a decrease (slight, but a decrease) in the number of heart transplantations, from 294 to 287 (2.3%). Looking on the brighter side, the number of patients waiting for a heart transplant at the end of last year fell from 111 to only 84, a decrease of 25% that is unprecedented in terms of the magnitude. Its coexistence with a stabilized transplant activity warrants an analysis of the cause-and-effect relationship, which we will address later on.

A superficial examination of the situation could lead us to consider that, since the age of the donors is increasingly greater, they are becoming progressively less apt for the transplantation of thoracic organs, which are more delicate than abdominal organs because of certain requirements with regard to age and vascular status. However, this fits in poorly with the fact that lung transplantation, which is even more selective than heart transplantation in terms of donors, has increased by no less than 16.7% during 2005. The heart transplant activity in Spain reached a high of 353 procedures in 2000. Still, if we analyze the total number of donors under 55 years of age (the cutoff age for heart donation) during that period and compare it with the figure for 2005, we observe that, far from having decreased, it rose from 811 in 2000 to 819 in 2005. Thus, with a similar or slightly higher number of theoretically potential donors in terms of age, we are performing considerably fewer transplantations. Something is going on.

Factors Related to Recipients, Transplant Teams, and Organ Distribution

There are several reasons for this decrease. Some are clearly positive and others, of course, are less so. On the one hand, the heart is the only solid organ whose necessities, far from increasing in geometric progression, have been tempered over the course of time, mostly as a consequence of improvements in the treatment of heart failure. However, it is also true that if we had a larger donor pool, the cases in which transplantation was indicated would also increase.³ We only have to take a look at last year's ONT report⁴ to see that the number of cases in which transplantation was indicated among the residents of the different Spanish autonomous communities ranged from 25.9 to

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4.2 per million population, with a mean of 11.4 and a difference of 6 to 1.

Obviously, these figures are not a consequence of epidemiological differences involving heart diseases; rather, they reflect a variability in clinical practice that, in turn, has quite a lot to do with the degree to which the population has access to transplant centers and the distance between the closest center and an individual's home. It appears to be no coincidence that the communities of the Balearic Islands, the Canary Islands, Castilla-La Mancha, and La Rioja, all of which lack a transplant team, are those in which there were the least number of cases in which transplantation was indicated in 2004,⁴ and we have no reason to think that the health of the hearts of those citizens is markedly better than that of the inhabitants of regions in which there are transplant teams. This fact, known since the ONT has had access to the corresponding information, at the beginning of the nineties, is one of the factors that has had the greatest influence on the development of new teams, a decision made by each autonomous community, first promoted by the professionals in the region and traditionally challenged by those who were already performing transplantation.⁵

True, we are dealing with a number of potential recipients that at least has not grown, as in the case of the transplantation of other organs. The waiting list figures at the end of 2005 are equivalent to those of 10 years ago, a circumstance that is inconceivable in the case of lung or liver. On the other hand, the difference in the disease severity in the patients we are dealing with is evidenced by the changes in the incidence of urgent transplantation. Whereas during the nineties it remained around 20% and in 2000 it was 16%, during 2004 it reached 34.7%, that is, 1 in every 3 transplantations.

The limitation to elective procedures, on the one hand, and the present number of teams, on the other, has fragmented the waiting lists, leaving them chronically short for most of the teams. Just think about this: on 31 December 2005, the 83 patients mentioned above were distributed among 17 teams, that is, a mean of less than 5 patients per team, although with marked differences (which means that, in some hospitals, they are practically symbolic). If we consider the distribution according to blood groups and the differences in size, it is understandable that the possibility of "marrying" donor with recipient within the same community in which the donation occurs is increasingly complicated. This, together with the increase in urgent procedures, means that air transport is required much more frequently than for any other type of transplantation.

Here we have a very important cause for potential improvement. There is a difference between a donation in the same city or community and one that requires a flight of over an hour, especially when one or more evaluations have been carried out previously by the local or nearby team, which sometimes takes hours, only to

say in the end that they "prefer to wait for another more suitable donor", when there is no longer a possibility, or a very limited one, to make arrangements with another less selective team. Evidently, we are talking about hearts that do not meet all the "ideal" requirements (with the "optimal" donor, there are usually no problems), but that, in any case, would have been transplanted by other teams with broader criteria or with greater pressure on the waiting list. This decision may make all the sense in the world from the point of view of the specific patient awaiting the transplant (which is usually the only stance considered by the team), but it is, at the very least, frustrating for coordinators, and especially so for those of us who see the problem from a central standpoint and know that it is repeated more frequently than would seem reasonable.

This account of the events, difficult to translate into objective figures, but as real as life itself, is made worse by a circumstance that is also perceptible from a central standpoint, and perhaps less so from the sidelines: the multiplication of interlocutors making decisions. Whereas, in the initial years (and this still occurs in some teams), a given person always assessed the donors and made the decisions as to their viability, this responsibility now falls in the first instance on an ever greater number of cardiologists who have to make decisions, based on less experience, without an overall view of the matter, but with a sword of Democles hanging over their heads: if the graft does not function, the first consideration is that the heart was not suitable.

Here we enter the Gordian knot of the problem we are analyzing. If the cardiologist or surgeon says the heart is not suitable, his or her clinical judgment is going to be the "standard," because no one will be able to demonstrate the opposite. Only if another team accepts it, implants and it functions (which, on the other hand, often occurs) does it become evident that the assessment was not entirely correct. In the opposite situation (the acceptance of a "suboptimal" heart that may not function), there is, in contrast, a personal and professional price to be paid that not everyone assumes in the same way. It again gives rise to the dilemma "What is best for my patient versus greater possibilities for all the patients on the waiting list, and even those who don't make it on the list due to a lack of expectations."

The pressure associated with this aspect can be appreciated through a curious datum: in the latest report of the Spanish Heart Transplant Registry,⁵ the expression "acute graft failure" appears no less than nine times (not counting other synonyms), and the idea that "the attempt must continue to be made to reduce it" was especially stressed, a fact that points toward stricter donor selection.

However, consciously or unconsciously, this selection is being made even now. Two circumstances evidence this. On the one hand, what we said above concerning the transplant activity: in 2000, with 811 donors of less

than 55 years of age, 353 transplantations were performed, while in 2005, with 819, 287 were carried out, nearly 60 fewer. On the other hand, according to Registry data,⁵ despite the fact that the incidence of urgent transplantation rose to an all-time record of 35% in 2004, early mortality (within the first 30 days of transplantation) decreased to an also all-time minimum of 10%. Without excluding improvements in the procedure and in the teams performing it, more functioning grafts in patients with much greater disease severity would appear to indicate a considerable rate of correct selection of the transplanted organs.

Donation-Related Factors

From the point of view of the donors, an aspect on which the article by Chamorro et al² focuses, the group at Hospital Puerta de Hierro provides a series of highly interesting data. On the one hand, 30% of the exclusions of heart donors are attributed to ventricular dysfunction. This occurs in a hospital with a maximum experience in this treatment and with a coordination team and intensive care unit that are especially knowledgeable and interested in the process.

The overall situation is a far cry from this one. Saying the following in a cardiology journal is not going to be very popular, but the generalization of the use of echocardiography, at any hospital and at all hours, as a method of assessing individuals in a situation of brain death constitutes a significant factor in the loss of donors. One of the factors that differentiates Spain from other countries in terms of the number of donors is the considerable contribution of small hospitals to the organ donor pool. Just with the donors generated in hospitals with transplant teams, our country has more donors per million population than the United Kingdom or Germany.

This has led to the existence of 155 hospitals authorized to make donations, with their corresponding coordination teams, versus 17 hospitals in which heart transplantation is performed. According to data from 2005, only 35% of the acceptable hearts were generated at transplant centers, despite their being larger, where neurosurgery is performed and with the capacity to accommodate a larger number of suitable donors. The result is that two thirds of the selected donors (and higher percentages of potential donors) are evaluated by cardiologists who are not necessarily accustomed to managing these individuals, and moreover, at any time of day or night. Their report is going to determine whether or not a distant team decides to make the trip to examine the organ *in situ*. Any negative or doubtful finding which, on occasion, may be expressed in a clearly defensive manner, because of the waiting list and other conditioning factors that we described above, is going to lead to the refusal of the organ and its being counted as "unacceptable." How can we demonstrate the opposite? Mission: impossible. The only way to definitively prove

that a heart is suitable for transplantation is by employing it and seeing that it functions. Nevertheless, on the basis of the data provided here, we can at least raise certain doubts about those that are discarded day after day, especially if we go on to admit that the number of patients who could benefit from this treatment would be much greater if there were sufficient organs.⁶

It has long been known that brain death is frequently associated with a series of changes in myocardial contraction,^{1,6,7} attributable to a large extent to catecholamine release, and that these changes are often the reason for which the heart does not get transplanted. The most relevant aspect of this condition is its potential reversibility, in up to 75% of the cases when serial echocardiograms are performed.⁸ This clearly shows that a good number of hearts that probably would have been acceptable and not getting transplanted, a number that Chamorro and his group estimate at no less than 55 to 82 every year (the entire waiting list).¹ Needless to say, a large proportion of these hearts used to be implanted when echocardiography was not available at so many hospitals and at certain hours.

One interesting hypothesis, that probably has a lot of truth to it,¹ is that the simplification of the diagnosis of brain death after Royal Decree 2070/1999 came into effect means that the phenomenon of myocardial dysfunction is detected more frequently in the initial evaluation. This situation seems to be common; it is not well recognized, and we need to search for solutions because it makes us reject hearts from very young donors that very probably would have been transplanted had the examination been carried out a few hours later.

On the other hand, the natural trend in any type of transplantation is that the most active teams expand their criteria for the acceptance of donors.⁹ The case of the heart involves additional problems that implicate other organs, since it requires a more delicate evaluation that includes the use of techniques such as coronary arteriography, that are difficult or impossible to spread across the entire map of Spanish donation described above, especially on a 24-hour basis. It would be possible to advance along this road only at a few specific centers, although it seems reasonable that other approaches be explored first.

The Future: What Can Be Done?

The first step in the solution to any problem is to verify its existence and diagnose it properly. Perceiving that the accelerating rhythm of the transplantation of abdominal organs is not being matched by that of thoracic organs, the ONT initiated a process in 2005 that should lead to a progressive optimization of the donation procedure. A work group, comprised of representatives of all the actors in this complex process (clinicians, surgeons, intensivists, coordinators, etc), has been established to prepare guidelines for the maintenance of

the thoracic organ donor in the intensive care unit. This group, with the active involvement of the Spanish Society of Intensive Care, Critical Care, and Coronary Care Units has drawn up a series of recommendations that should be approved and implemented in the coming months. They will have the added value of focusing our attention on an aspect of our system of transplantation in which the room for improvement is manifest and for which we must find the most satisfactory solutions. The meetings to be held in 2006 with the thoracic organ transplant team will be a good opportunity to discuss all these aspects.

Organ donation constitutes a valuable asset that Spanish society puts in our hands for us to administer in the best possible way. Any weak point in the system should be carefully analyzed and corrected because there are many patients who can benefit from the gift of life contained in a transplant. A recent report¹⁰ calculated the life-years gained after an organ donation, and compared the survivals recorded in North American registries. A multiple organ donation represents no less than 55.8 life-years gained and, in terms of single organs, heart donation and transplantation results in an average of 14.5 years wrested from death. It is difficult to picture, simply and schematically, the possible significance of the decisions we are making every day so that a patient on a waiting list can go on living.

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