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# Resuscitation

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## Letter to the Editor

# Assessment and treatment of ischemia reperfusion injury: The real challenge of uncontrolled donation after circulatory death



Sir,

We read with great interest the letter by Manara et al.<sup>1</sup> who elegantly underscore that organ donation should be considered routinely as part of the patient's end of life care in an out-of-hospital (OHCA) integrated program, including extracorporeal membrane oxygenation (eCPR) and uncontrolled donation after circulatory death (uDCD) pathways. Though an uDCD program handles several challenges, the large potential of uDCDs should induce further efforts to overcome these difficulties, which are organizational, ethical, cultural and even related to local laws.

Though in Europe Spain has the largest uDCD program,<sup>2</sup> in recent years uDCD pathways were implemented also in Italy. From the called "Alba program" including both controlled and uncontrolled DCDs, in Milan since September 2015 a DCD program specific for liver transplantation has started with recent reports of preliminary data.<sup>3</sup> In Florence, since 2016, an uDCD pathway has been established within the OHCA program and promising initial results were reported.<sup>4</sup>

The Italian scenario is characterized by two main peculiarities/obstacles. Firstly the declaration of death based on circulatory criteria requires a no-touch period of at least 20 min, much longer compared to the 5 min accepted in other European countries. Secondly donor hospitals are generally logistically distant to transplant centers. These two "geographic" factors may affect the reperfusion-ischemia injury on splanchnic organs and in Italy, much more than in other countries, reperfusion strategies (in vivo and ex vivo) are mandatory in uDCDs. Nevertheless, existing data strengthen the growing evidence that uDCD programs are feasible also in Italy (despite a longer no touch period) and lead to a substantial increase in the potential donor pool.

Normothermic regional perfusion (NRP) is currently used by Italian uDCD hospitals.<sup>3-5</sup> The main advantages of nRP are that it restores blood after the determination of death, regenerating cellular energy substrates, and that it allows the assessment of organ viability, even if, to date, there is no reliable metrics during nRP to determine whether a splanchnic organ is safe to be ex situ perfused or to be transplanted. When investigating the effects of ischemia during nRP by the dynamic

variations of transaminases and creatinine in 17 uDCDs,<sup>5</sup> creatinine values did not significantly changed while transaminases progressive increased. These data strongly suggested that nRP does affect splanchnic organs being the liver sensitive to hypoperfusion.

Viability assessment during nRP is certainly an important goal but in uDCDs ex vivo perfusion is necessary for splanchnic organs to better quantify the ischemic-reperfusion injury after in vivo perfusion and, mostly, to assess residual organ function.

The impact that an uDCD program can have on the pool of potential donors necessarily stems from the understanding of the ischemia reperfusion injury and of the potentials of reperfusion techniques to restore/repair organ damage after ischemia-reperfusion.

## Conflict of interest

None.

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