SUPPLEMENTARY MATERIAL

Supplementary material (Video 1 and Supplement 1) is available at EJCTS online.

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References

Cerebral ischaemia is a major concern in various fields. First, cardiac arrest, witnessed or unwitnessed, is a huge health problem [2]: 450 000 patients are concerned every year in the USA. The result of the present management of cardiac arrest is quite disappointing: the mortality rate is extremely high (85–95%) in the witnessed cardiac arrest and is minimally improved by efforts restoring satisfactory cerebral perfusion as soon as possible. The training of the general population to improve cardiac resuscitation promoted by the Red Cross, the extensive availability of automatic defibrillators in public places, the stationing of mobile emergency units and trained paramedics throughout big cities, and the development of the use of emergency percutaneous cardiopulmonary bypass have not dramatically improved the survival. In addition, the extremely high rate of permanent neurological damage in the survivors of witnessed cardiac arrest is a huge healthcare problem. The figures are even worse in the group of patients sustaining an unwitnessed cardiac arrest. Unfortunately, the progress made over the past 20 years in the results of the treatment of cardiac arrest is minimal [3]. The recent development in the use of various mechanical circulatory systems in this indication has not much improved the situation. The recently published experience in Paris confirms these poor results [4]: 4% survival without any neurological complications in 51 cases of out-of-hospital cardiac arrest has led to the restriction of the indication for percutaneous mechanical support to very rare cases. What is more, new difficulties have emerged: the worst and the most difficult to handle is the patient ‘recovering’ from a cardiac arrest, stable either spontaneously or because of some type of mechanical circulatory support, who presents major neurological damage in the postresuscitation period. Only time and permanent monitoring enable us to distinguish between severe cerebral damage, which eventually will be reversible, and brain death. This difficulty is one of the strongest reasons to support the concept of restricting the modalities of circulatory support to percutaneous cardiopulmonary bypass and of contraindicating the use of expensive ventricular circulatory support systems as a first-line technique.

Cerebral stroke is the second clinical situation where progress is needed. Huge efforts have been made in the developed countries to improve the outcome of patients sustaining a cerebral stroke. Stroke centres equipped and serviced by trained specialists 24 h a day have been organized to allow rapid diagnosis and immediate revascularization. Nevertheless, the same disappointing figures are observed in the efficacy of these stroke centres: despite the rapidity of the medical intervention including early diagnosis and reperfusion as early as possible, the rate of permanent neurological sequelae remains high.

In this context, Allen and colleagues propose a totally different approach. It is based on the hypothesis that an ischaemic/reperfusion injury is a general phenomenon affecting every organ. The basic idea is that controlled reperfusion is a unifying treatment for the general biological process of ischaemia/reperfusion injury. Then, the controlled reperfusion of the brain should minimize the cerebral consequences of the ischaemic/reperfusion injury, as does the controlled reperfusion of the myocardium following a period of myocardial ischaemia due to coronary artery occlusion or poor myocardial protection during cardiac interventions. Consequently, rapid conventional cardiac resuscitation, which provides uncontrolled reperfusion, should be avoided and an emergency percutaneous cardiopulmonary bypass, providing controlled reperfusion, should be started.

The validation of this new hypothesis is for many reasons quite a challenge. First, there are few models available to test the hypothesis and the first step of the authors is to design and validate a good model of isolated cerebral ischaemia [5]. The brain has to be preserved from the whole-body response to the cardiac arrest. Actually, cardiac arrest itself is responsible for a large whole-body inflammatory response and the release of cytokines impacting the cerebral perfusion itself. Second, evaluation of cerebral function is itself difficult. There are few parameters that are relevant in the immediate assessment of the impact of cerebral ischaemia on function. The techniques used today reflect local abnormalities at the site of the measurements and they do not permit a correct assessment of general brain function. Thirdly, cerebral function is affected by the anaesthetic conditions. Finally, the modalities of the controlled reperfusion which have been proposed for optimal myocardial reperfusion are probably not optimal for cerebral reperfusion and they have to be selected: we need to define the roles of pressure, reperfusion flow, temperature, chemical characteristics (pO2, pCO2, pH etc.), additives (glucose, insulin, glutamate etc.) and pharmacological agents (calcium-blocking agents, steroids etc.), and the modalities of cerebral reperfusion, either isolated or through the general circulation.

This means a lot of experimental studies. A first group of experiments [6] focuses on the importance of perfusion pressure. A good balance has to be found to permit good cerebral reperfusion and to avoid direct damage due to excess pressure responsible for tissue oedema. The second group of experiments deals with the role of pulsatility [7]. Many more experiments are necessary to define the optimal options in terms of what is perfused. Finally, large clinical studies will be required to evaluate the impact of this new approach in the management of cardiac arrest and the other clinical circumstances where cerebral function is at risk (stroke, carotid and aortic arch surgery etc.). A last issue to be solved will be to evaluate the higher neurological functions following a prolonged cardiac arrest and a successful recovery: only clinical experience will make sure that the recovery of brain function includes the recovery of normal intellectual and psychological performances.

The methodology used by the authors mimics perfectly well the outstanding work performed by Gerald Buckberg over the past 30 years a very rigorous, step-by-step approach to the complex problem of myocardial ischaemia recovery. Today, his group is addressing the most challenging problem, the recovery of the ischaemic brain. This approach developed in these first four papers clearly confirms the words of Paul Valéry: ‘the real mentors are those who show what is possible in the domain of the impossible’.

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REFERENCES


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