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The ongoing MESAMI translational research program.

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Purpose: Despite the improvement of pharmacological and surgical therapies, the mortality related to ischemic heart failure remains high. During the last years, bone marrow-mesenchymal stem cell (BM-MSC) therapy has been proposed as a novel approach for the prevention and therapy of heart failure. Intramyocardial injection allows concentration of grafted cells within the injured zone. However, a major problem of with intraparenchymal route of administration is the early death of most of grafted cells. The goal of the MESAMI program is to evaluate the effect of intramyocardial administration of BM-MSC preconditioned or not with the pineal hormone melatonin in ischemic cardiomyopathy.

Methods and Results: Our preclinical investigations have designed a preconditioning strategy of BM-MSCs with the melatonin that significantly increases survival and efficacy of grafted cells in animal models of myocardial ischemia. Melatonin treatment significantly ameliorates the beneficial effects of BM-MSC on the recovery of cardiac function. In the mean time, we started a phase I clinical trial in patients with severe ischemic cardiomyopathy and no option of revascularization, using the NOGA XP system to guide injections into the myocardium. Based on our basic research results, we are developing a multicenter phase II trial on the effects of intramyocardial administration of melatonin-preconditioned BM-MSC in patients with chronic ischemic cardiomyopathy.

Conclusion: The ongoing MESAMI program is representative of a translational research program in France.

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Impact of immediate coronary angiography and new reanimation techniques in cardiac arrest patients.

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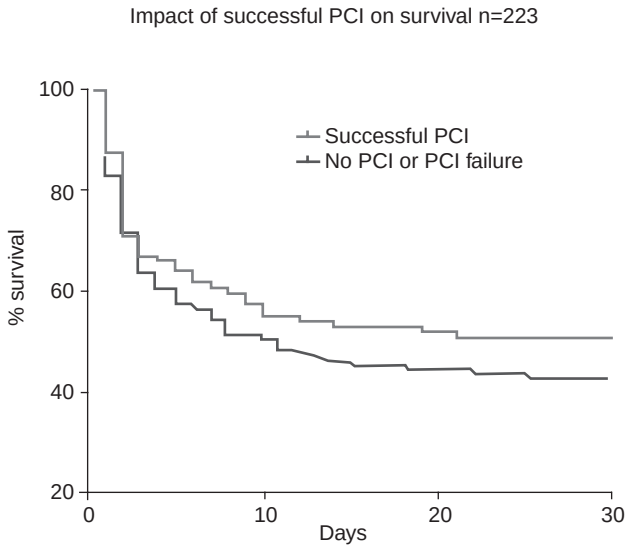
Background: Prognosis of patients surviving having an out-of-hospital or an in-hospital cardiac arrest is still very poor. Immediate coronary angiography with successful angioplasty has shown to improve prognosis of these patients. Nevertheless this strategy in the setting of new reanimation techniques using hypothermia or cardiac assistance has not yet been evaluated.

Aim: To evaluate the impact of coronarography and ad hoc angioplasty on survival rate.

Methods: The Pitié-Salpêtrière registry included 328 consecutive patients who survived a cardiac arrest and were transferred to the cath-lab for emergency coronary angiography followed by ad-hoc PCI and state-of-the art critical care techniques. We present here intermediate results with the follow up of 223 consecutive patients.

Results: Most (65.7%) cardiac arrest survivors had angiographic coronary artery disease (at least one lesion >70%), with an attempted angioplasty in 49.1% of the total patients and in 75% of patients with coronary artery disease. Angioplasty was successful in 82.4% of attempted PCI. Total hospital survival rate was 43.8% when it was 45.7% in patients with CAD and 40.8% in patients without CAD, p=0.1with non adjusted HR 1.09 (95% CI 0.7-1.6). Survival rate was 48.3% in patients with successful PCI and 40.6% in patients without PCI or PCI failure, p=0.3 with non adjusted HR 1.2(95% CI 0.8-1.8). Complete follow up pf the cohort is pending.

Conclusions: Two third of cardiac arrest survivors present with angiographic coronary artery disease and undergo 75% of attempted PCI. In this intermediate analysis presence of CAD and successful PCI provided trend in a better survival but were not significantly associated with a better outcomes.



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Resistance to antiplatelet therapy in the elderly, a real concern. Results of the senior platelet study

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Background: Dual antiplatelet therapy effect on platelet inhibition in elderly patients (>75 y/o) is unknown as this growing proportion of ACS are often excluded from clinical trials

Aim: To compare on-treatment platelet reactivity under dual antiplatelet therapy of elderly (>75 yrs) vs. younger patients (< 75yrs).

Methods: We included 652 coronary patients treated by aspirin and clopidogrel in whom platelet response was assessed by light transmission aggregrometry with measure of Maximum (MPA) and Residual Platelet Aggregation (RPA) and VerifyNow with PRU. The population was divided in 5 age categories and compared with elderly patients >75 yrs. Rates of non-response were established using admitted definitions.

Results: The mean MD of clopidogrel and aspirin were 86.6mg and 80.6 mg in patients <75 y/o respectively, and 81.8 mg and 78.6 mg in the elderly. On-clopidogrel platelet reactivity was higher in elderly patients when compared to younger patients whatever the test used (figure). The rate of non-responders was 37.1% in the 105 elderly patients when assessed by PRU>235 and 19,01% in the 547 younger patients (<75 y/o; p<0,001). Results were even more striking when RPA was considered with 67.3% non-responders in the elderly patients vs. 22.8% in the 547 younger patients; p<0,001). Mean ARU was similar in both groups with 440U in patients under 75 y/o vs. 452U in elderly (p=0.8), but the mean AA induced MPA was 5.5% in patients under 75 y/o vs. 10.4% in elderly (p=0.01). The rate of non-response was 6.25% and 15% with LTA (p=0.001).

Conclusions: Elderly patients have higher levels of on-treatment platelet reactivity for both clopidogrel and aspirin and a 2-fold increase in the rate of non-responders to clopidogrel and a 3-fold increase of non-responders to aspirin, suggesting that they should not be undertreated.