Sonothrombolysis delivered before percutaneous coronary intervention improves myocardial salvage in ST elevation myocardial infarction

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Background: Sonothrombolysis (STL) is the application of high mechanical index ultrasound whilst infusing an ultrasound contrast agent. Prior studies have shown that STL delivered pre & post primary percutaneous coronary intervention (pPCI) can reduce infarct size, and improve myocardial salvage in the setting of ST Elevation Myocardial Infarction (STEMI). However, it remains unclear whether this benefit is proportionately dependent on the amount of STL delivered, and whether the timing of STL relative to pPCI is important.

Purpose: To determine if there is a dose and time dependent relationship between sonothrombolysis delivery and myocardial salvage in patients presenting with STEMI.

Methods: We conducted a double-blind, pilot randomised controlled trial of STEMI patients (symptoms <6 hrs, age 30-80). Patients were randomised (1:1:1) into 3 arms; Group 1 received STL pre & post pPCI, Group 2 received sham echo pre and STL post pPCI, while Group 3 received Sham echo pre and post pPCI. Measured endpoints were Infarct Percent and Myocardial Salvage Index (MSI) assessed with CMR at day 4±2 and 6±1 months. We performed a regression analysis using R Version 4.2.2 to determine if the number of delivered STL cycles were associated with an improvement in myocardial salvage.

Results: 51 patients (Age 60, Male 82%) were recruited into Group 1 (n=16), Group 2 (n=19) or Group 3 (n=16). MSI was higher in Group 1 (79% [64, 85]) than Group 2 (51% [45, 70]) and Group 3 (48% [37, 73]) (p=0.047). Regression analysis (Figure 1) showed a non-significant trend towards improved myocardial salvage with more delivered cycles (β=0.32 [95%CI -0.15, 0.80]). Subgroup analyses of post pPCI STL (Figure 2) shows a fixed and sustained benefit in myocardial salvage with pre & post pPCI STL delivery, compared to post pPCI STL delivery alone. Given the regression lines for Group 1 and 2 are approximately parallel, we compared alpha intercept values to determine that pre & post PCI STL conferred an additional 17 percentage points (75% versus 58%) of myocardial salvage compared to post pPCI STL alone. No major adverse cardiac events occurred amongst included participants.

Conclusion: Pre pPCI sonothrombolysis appears to be an essential component of improving myocardial salvage in the REDUCE Pilot trial, and may improve myocardial salvage by an additional 17% compared to post pPCI STL alone. This benefit is independent of post pPCI sonothrombolysis duration.

Figure 1: The relationship between number of delivered cycles of sonothrombolysis and myocardial salvage index.
Figure 2: Group 1 and Group 2 sub-analysis