Safety of Selective Intracoronary Hypotheria during Primary Percutaneous Coronary Intervention in Patients with Anterior St-Elevation Myocardial Infarction

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Tweet/handle: Mohamed El Farissi: @MohamedFariss19; Selective intracoronary hypothermia is a novel treatment designed to decrease infarct size and appears safe in patients with anterior STEMI

ABSTRACT

Background Selective intracoronary hypothermia is a novel treatment designed to reduce myocardial reperfusion injury and is currently being investigated in the ongoing randomized controlled EURO-ICE trial (ClinicalTrials.gov NCT03447834). Data on the safety of such procedure during primary percutaneous coronary intervention (PPCI) are still limited.

Objectives This study sought to determine the safety of selective intracoronary hypothermia during PPCI in patients with anterior ST-elevation myocardial infarction (STEMI).

Methods The first 50 patients with anterior STEMI, treated with selective intracoronary hypothermia during PPCI were included in this analysis and compared for safety to the first 50 patients randomized to the control group receiving standard PPCI. In-hospital mortality, occurrence of rhythm- or conduction disturbances, stent thrombosis, onset of heart failure during the procedure and subsequent hospital admission were assessed.

Results In-hospital mortality was 0%. One patient in both groups developed cardiogenic shock. Atrial fibrillation occured in 0 vs 3 patients *(p=0.24)* and ventricular fibrillation occurred in 5 vs 3 patients *(p=0.72)* in the intracoronary hypothermia group and control group, respectively. Stent thrombosis occurred in 2 patients in the intracoronary hypothermia group, one was intraprocedural and the other occurred following interruption of dual antiplatelet therapy consequent to an intracranial hemorrhage 6 days after enrolment. No stent thrombosis was observed in the control group *(p=0.50)*.

Conclusions Selective intracoronary hypothermia during PPCI in patients with anterior STEMI can be implemented within the routine of PPCI and seems to be safe. The final safety results will be reported at the end of the trial.

KEY WORD: STEMI, selective intracoronary hypothermia, myocardial reperfusion injury, infarct size, procedural safety.

CONDENSED ABSTRACT

The first 50 patients with anterior STEMI, treated with selective intracoronary hypothermia during PPCI in the randomized controlled EURO-ICE study were included in this analysis and compared for safety to the first 50 patients randomized to the control group receiving standard PPCI. In-hospital mortality was 0%. One patient in both groups developed cardiogenic shock. Atrial fibrillation occured in 0 vs 3 patients and ventricular fibrillation occurred in 5 vs 3 patients in the intracoronary hypothermia group and control group, respectively. Stent thrombosis occurred in 2 patients in the intracoronary hypothermia group and in none of the patients in the control group. Selective intracoronary hypothermia during primary PCI in patients with anterior STEMI can be implemented within the routine of primary PCI without safety concerns.

ABBREVIATIONS AND ACRONYMS

STEMI	ST-elevation myocardial infarction
PPCI	primary percutaneous coronary intervention
IS	infarct size
MaR	myocardium at risk
VF	ventricular fibrillation
AF	atrial fibrillation
ST	stent thrombosis
IPST	intra-procedural stent thrombosis

INTRODUCTION

Primary percutaneous coronary intervention (PPCI) has become the cornerstone of treatment in patients with acute myocardial infarction (AMI) and has significantly improved outcome (1). However, in a number of patients, reperfusion injury may undo a considerable part of the recovery of the ischemic myocardium achieved by PPCI (2,3). Consequently, preventing myocardial reperfusion injury is seen as the next challenge in patients with AMI, especially in the case of ST-elevation myocardial infarction (STEMI). Therefore, the importance of endeavors to limit myocardial reperfusion injury, in order to decrease infarct size (IS) and further improve clinical outcomes, is undisputed (2).

Selective intracoronary hypothermia is a novel therapy intended to reduce myocardial reperfusion injury and has shown beneficial effects in animal studies (4). In humans, however, such therapy is not trivial and its feasibility has been investigated only recently in a small pilot study (SINTAMI) (5). So far, no clinical outcome data are known. Presently, the effectiveness of selective intracoronary hypothermia to decrease IS is being investigated in 200 patients in the prospective, randomized controlled EURO-ICE trial (ClinicalTrials.gov NCT03447834) (6).

For such a new and experimental therapy, monitoring of safety is paramount. In the SINTAMI study, Otterspoor et al investigated the safety of selective intracoronary hypothermia in 10 patients with STEMI (5). In 2 out of 4 patients with inferior STEMI and an occluded right coronary artery, symptomatic AV conduction disturbances were observed, one of which necessitated treatment with a temporary pacemaker. In 6 patients with large anterior STEMI, no complications were observed. For this reason, only patients with anterior STEMI are being recruited in the EURO-ICE trial (6). Upon approval of the study by the institutional review board (IRB), interim analysis for safety of the procedure was mandated after 50

patients had been treated by selective intracoronary hypothermia. Furthermore, an independent data safety and monitoring board (DSMB) oversees the trial and interim analyses will be performed at the discretion of the DSMB (6).

Accordingly, the present study evaluates the prespecified procedural safety in the first 50 patients with anterior STEMI in the ongoing EURO-ICE trial, treated with selective intracoronary hypothermia during PPCI in comparison to the first 50 patients randomized to the control group receiving standard PPCI.

As the investigators and authors of this paper do not have access to outcome data by design, this report is limited to the predefined safety parameters.

METHODS

From the ongoing EURO-ICE trial, the first 50 patients with anterior STEMI, treated with selective intracoronary hypothermia during PPCI were included in this safety analysis and compared to the first 50 patients randomized to the control group receiving standard PPCI. EURO-ICE is a 1:1 randomized controlled European multicenter trial, evaluating the effect of selective intracoronary hypothermia on IS, as measured by cardiovascular magnetic resonance imaging (6).

The study was approved by the institutional review board in all participating centers. Patients between 18 and 80 years old with anterior STEMI and summed ST-segment deviation on the electrocardiogram of at least 5 mm were screened for eligibility. Cardiac catheterization was performed using femoral or radial access. Eligibility was established in case of an occlusion in the proximal or mid segment of the left anterior descending (LAD) artery with Thrombolysis in Myocardial Infarction (TIMI) grade flow 0 or 1. Oral consent was obtained in the catheterization laboratory immediately after angiography of the left coronary artery (LCA). Hereafter, the patient was randomized to the intracoronary cooling

protocol during PPCI or to standard PPCI. Written informed consent was obtained later during hospital admission.

Selective intracoronary hypothermia – instrumentation (Figure 1)

A 6 French guiding catheter was positioned in the LCA and the occlusion in the LAD artery was crossed by a regular guidewire. Immediately thereafter, a properly sized over-the-wire balloon (OTWB) was advanced and inflated to 4 atmospheres at the site of the occlusion to secure persistent occlusion of the LAD. A pressure/temperature sensing wire (PressureWire™ X, Abbott, Saint Paul, MN, USA), was connected to the CoroFlow © v3.0 software platform (Coroventis, Uppsala, Sweden) and introduced into the ostium of the left main coronary artery. After equalization of the pressures with automatic 'zeroing' of the body temperature, the PressureWire™ X was advanced alongside the OTWB into the distal LAD, for which purpose the balloon was deflated for a few seconds. The regular guidewire was then retracted from the central lumen of the OTWB so that this lumen could be used for infusion of saline.

Selective intracoronary hypothermia – cooling (Figure 2A/B and 3)

Selective intracoronary hypothermia consisted of 2 phases, the 'occlusion' phase *(Figure 2A)* and the 'reperfusion' phase *(Figure 2B)*.

During the occlusion phase, the OTWB remained inflated with 4 atmospheres. This prevented reperfusion (and with it reperfusion injury). During this phase, saline at room temperature (±22º C) was infused through the central lumen of the OTWB for a duration of 7 to 10 minutes. The intracoronary target temperature was 6 to 8º C below body temperature. Due to the temperature gradient between coronary artery and myocardium at risk (MaR) in this phase (cold transfer by conduction), the temperature of the MaR is 31-33º C (7).

In the reperfusion phase, the OTWB was deflated and blood flow was (partially) restored. To compensate for the mixture of warm blood flow in the MaR, cold saline (±3-4º C) was used for infusion during this phase. The switch from saline of 22º C to saline of 3º C was made just before the deflation of the balloon. The coronary target temperature was 4 to 6º C below body temperature and the duration of this phase was 10 minutes. Since there is no relevant temperature gradient in this phase between the coronary artery and the corresponding MaR (cold transfer by convection), this translates into a myocardial temperature of 31-33º C (7).

After the reperfusion phase was finished, the OTWB was retracted and the PressureWire™ X could be used as a guidewire for placement of a stent. If the operator wished to use a regular guidewire to finish the procedure, this guidewire could be inserted and advanced into the distal LAD through the central lumen of the OTWB. Thereafter, the OTWB was retracted using standard techniques.

As an alternative to the use of a regular wire and OTWB, it was also possible to start the procedure immediately with the PressureWire™ X to cross the occlusion and to advance a specific monorail balloon-infusion catheter (CoolCell®, Hexacath, Paris, France) over the PressureWire™ X to the site of the occlusion and inflate it to 4 atmospheres. No second wire was neccesary in that case making the technical performance of the procedure easier (6). The CoolCell® catheter is not CE-approved yet and is used within some of the participating centers as an investigational medical product. The CoolCell® catheter was used in 15 out of the 50 patients included in this analysis.

After the cooling procedure, stenting was performed, and the procedure was completed according to standard care. During the occlusion phase, opioids and/or

benzodiazepines may be used if indicated to reduce chest pain. All other medical treatments, peri-procedural and at follow up, are identical to normal standard of care.

Control group – standard PPCI

Patients in the control group received PPCI completely according to standard techniques and according to the routine in the participating centers.

Assesment of complications and safety

During the procedure, clinical, hemodynamic, and electrocardiographic variables were obtained. Duration of infusion, coronary temperature, and total amount of saline used per phase were recorded in patients treated with selective intracoronary hypothermia. Special attention was paid to the occurrence of hypotension, rhythm- or conduction disturbances, and the effect of the cooling procedure on systemic temperature. TIMI grade flow at the end of the procedure and intraprocedural stent thrombosis (IPST) were assessed.

During the subsequent hospital admission, the occurrence of rhythm disturbances, stent thrombosis (ST), onset of heart failure, including the intravenous administration of diuretics and/or inotropes/vasopressors, and mortality were reported by site investigators and compared between both groups.

Statistics

Statistical analyses are presented in a descriptive manner. Normally distributed data are reported as mean and standard deviation (SD), skewed distributions as median and interquartile ranges (IQR). Binary variables and outcomes are presented as absolute numbers and percentages and will be compared by applying a chi-squared test or Fisher's exact test to a 2x2 table of binary events/group. A Mann-Whitney U test is used to compare medians across both groups. A paired, two-tailed t-test or Wilcoxon Signed Rank test are used to

compare paired values as appropriate depending on their distribution. A p value of <0.05 is considered statically significant. IBM® SPSS® Statistics Version 25 was used for all statistical analyses.

RESULTS

Baseline characteristics

The patients were included between January 2019 and January 2021 in 6 European heart centers. The baseline characteristics are presented in *Table 1*. The median age of the patients was 62.1 vs 64.9 years *(p=0.73)* and 45 vs 41 patients were male *(p=0.25)* in the intracoronary hypothermia group and control group, respectively. Median ∑ST-deviation on the classifying electrocardiogram was 16 millimeters vs 13 millimeters *(p=0.26)* in the intracoronary hypothermia group and in the control group, respectively.

Angiography revealed the culprit occlusion in the proximal LAD (syntax segment 6) in 30 vs 26 patients and in the mid LAD (syntax segment 7) in 20 vs 24 patients *(p=0.42)* in the intracoronary hypothermia group and control group, respectively. TIMI grade flow pre-PCI was grade 0 in 42 vs 45 patients and grade 1 in 8 vs 5 patients *(p=0.37)* in the hypothermia group and control group, repectively. Symptom onset-to-balloon time was slightly shorter in the hypothermia group compared to the control group, 2 hours and 23 minutes vs 2 hours and 44 minutes *(p=0.03)*, respectively. Door-to-balloon time was slightly longer in the hypothermia group compared to the control group, 30 vs 24 minutes *(p<0.001)*, respectively. This indicates that an additional 6 minutes was needed for the instrumentation required for the cooling procedure. In the intracoronary hypothermia group, symptom onset-to-balloon time and door-to balloon time are taken up to the start of the first balloon inflation, i.e. excluding the duration of the occlusion phase.

Selective intracoronary hypothermia (Table 2)

Target temperature was achieved within 104 seconds (IQR 17 – 165) after start of infusion. The duration of the occlusion phase was 8.00 minutes (IQR 7.00 – 10.00). Median intracoronary temperature during this phase was -6.47º C (IQR -6.00 – -7.00) compared to baseline and the tympanically measured systemic temperature fell by -0.20º C (IQR 0.00 – -0.60, *p=0.001*). The total infused volume saline at room temperature was 162.5mL (IQR 132.5 – 200.0) at a rate of 20 mL/min (IQR 20 – 22). No change was observed in heart rate during the occlusion phase. Compared to baseline, mean arterial pressure (MAP) increased during the occlusion phase, 83 mmHg (IQR 71 – 95) vs 92 mmHg (IQR 76 – 110) *(p<0.001)*, respectively *(Figure 4)*.

The duration of the reperfusion phase was 10.00 minutes (IQR 9.00 – 10.00). During this phase the intracoronary temperature was -6.44º C (IQR -5.29 – -7.59) compared to baseline. Tympanic temperature only changed by -0.10 º C (IQR 0.10 – -0.70, *p = 0.012*) compared to baseline. Total volume of cold saline used in the reperfusion phase was 147.0 mL (IQR 128.0 – 205.0) at a rate of 17 mL/min (IQR 14 – 20). Heart rate did not change, but MAP increased slightly compared to baseline (91 mmHg, IQR 70 – 110, *p=0.04*) *(Figure 4)*.

In those 15 patients in whom the CoolCell® catheter was used, door-to balloon time was shorter than in those 35 patients in whom the OTWB was used, 27 minutes (IQR 23 – 30) vs 32 minutes (IQR 26 – 36) *(p=0.03)*.

Safety endpoints (Table 3A and B)

All patients survived to hospital discharge. Ventricular fibrillation (VF) necessitating defibrillation, occurred in 5 vs 3 patients *(p=0.72)*, at some point during the procedure in the intracoronary hypothermia group and in the control group, respectively. In the intracoronary hypothermia group, one patient had VF before saline infusion had started. In two patients VF occurred during the occlusion phase and in 1 patient VF occurred during the reperfusion

phase, immediately after balloon deflation, i.e. directly after reperfusion. And one patient had VF 10 minutes after the hypothermia protocol was completed. In the control group, 2 patients had VF before reperfusion and 1 patient had VF directly after reperfusion. In all but one patient in both groups, treatment with one direct current was sufficient to restore rhythm and circulation immediately. In one patient in each group, chest compressions were performed for a short duration of time in addition to direct current shock therapy. No other resuscitation procedures were required. None of the patients in the intracoronary hypothermia group had atrial fibrillation (AF), 3 patients (6%) in the control group had AF *(p=0.24)*.

There was no report on peripheral embolization and none of the procedures were complicated by air emboli. Post-PCI TIMI grade flow 2 or 3 was observed in 50 patients vs 47 patients *(p=0.08)* in the intracoronary hypothermia group and in the control group, respectively. Stent thrombosis (ST) was observed in 2 vs 0 patients *(p=0.50)* in the intracoronary hypothermia group and control group, respectively. In the intracoronary hypothermia group, one patient had ST while still in the catheterization laboratory. In the second patient stent thrombosis occurred after 6 days.

In both groups, one patient developed acute heart failure *(p>0.99)* for which intravenous diuretics, and vasopressive agents were used. In addition, the patient in the intracoronary hypothermia group required support by extracorporeal membrane oxygenation (ECMO) as a bridge to recovery. After 1 week, the patient was weaned successfully from ECMO.

DISCUSSION

The present study sought to investigate the safety of selective intracoronary hypothermia during primary PCI in patients with anterior STEMI, both periprocedural and

during the index admission. Our results do not raise specific concerns with respect to the safety of this novel procedure. Final safety results will be reported after the trial is completed.

When evaluating the safety of any investigational treatment in patients with STEMI, whether interventional or related to drugs, the question always remains whether a particular complication is the result of the investigational therapy or the underlying disease, i.e. anterior STEMI.

In the intracoronary hypothermia group, no difference was observed in heart rate, but a slight increase of the MAP during the cooling procedure compared to baseline was found. The total volume of infused saline was 325.0 mL (IQR 268.0 – 407.5) which was infused in 18.0 minutes (IQR 16.0 – 20.0). This fluid challenge, although much smaller than the total volume of saline used for systemic hypothermia (5), could be related to this increase of the MAP. No patients suffered from hypotension during the cooling procedure.

Tympanically measured systemic temperature during the cooling procedure decreased minimally in comparison with baseline (occlusion phase: -0.20º C, *p=0.001*; reperfusion phase: -0.10º C, *p=0.01*). Although statistically significant, this observation does not seem clinically relevant.

No difference was found for any of the predefined safety parameters between the intracoronary hypothermia group and the control group.

Although the overall complication rate of STEMI has fallen since the introduction of thrombolysis and PPCI, certain complications like VF or heart failure are still not infrequent. Large anterior STEMI patients are at highest risk for complications. In this study, primary VF occurred in 5 vs 3 patients *(p=0.72)* in the intracoronary hypothermia group and the control group, respectively. It has previously been described that anterior STEMI increases the risk of VF, with an odds ratio of 2.10 (95% CI 1.40 to 3.00) (8). All patients included in this

safety study had large anterior STEMI. In addition, pre-PCI TIMI grade flow 0 also increases the risk of VF, with an odds ratio of 1.65 (95% CI 1.14 to 2.40) (8). This applies to the majority of the included patients in this safety study (87%). Therefore, the incidence of VF in this study is not very high and in line with expectations. Remarkably, and in contrast to studies in AMI with systemic hypothermia (9), not a single case of atrial fibrillation was observed in the intracoronary hypothermia group vs 3 patients in the control group *(p=0.24).*

Definite ST occurred in 2 patients in the intracoronary hypothermia group and in none of the patients in the control group *(p=0.50).* Although studies have shown that hypothermia may promote platelet adhesion, activation and ultimately their aggregation, and may therefore increase the risk of ST, different circumstances under which hypothermia is achieved (systemic vs local, duration, depth) are indistinguishably associated to this prothrombotic phenomenon (10). We believe that selective intracoronary hypothermia does not increase the risk of ST as is supported by this analysis. One patient had IPST. Although excluded from the official Academic Research Consortium (ARC) definitions of ST, IPST is more prevalent in patients with STEMI and pre-PCI TIMI grade flow 0 or 1 (11), corresponding to the profile of all patients in this safety study. In one patient ST occurred after 6 days due to interruption of dual antiplatelet therapy after the patient suffered from an intracranial hemorrhage for which urgent craniotomy and evacuation of hematoma surgery was required. The patient made a full neurological recovery.

Finally, none of the patients died during the procedure or the subsequent hospital admission.

LIMITATIONS

The present report is an exploratory safety analysis and only contains predefined safety parameters as mandated by the IRB and DSMB. No outcome data were available yet to

the investigators and authors of this paper. Furthermore, bias due to a small sample size cannot be excluded.

Only patients with anterior STEMI and an occlusion of the proximal or mid LAD were investigated and these data cannot be extrapolated to inferior STEMI, where conduction disturbances are more common (5).

Nevertheless, these results are encouraging, but more definite evidence regarding safety of selective intracoronary hypothermia in patients with STEMI and effectiveness will be provided when the ongoing randomized controlled EURO-ICE study is completed.

CONCLUSION

This first report on the safety of selective intracoronary hypothermia during primary PCI in patients with anterior STEMI suggests that such procedure can be implemented safely during primary PCI without increased risk of complications. The ongoing randomized controlled EURO-ICE study will demonstrate whether selective intracoronary hypothermia will reduce IS and improve clinical outcome.

PERSPECTIVES

WHAT IS KNOWN?

Selective intracoronary hypothermia is a novel treatment, designed to reduce myocardial reperfusion injury and decrease infarct size in patients with STEMI.

WHAT IS NEW?

This safety study suggests that this technique can be implemented within the routine of primary PCI without safety concerns in patients with anterior STEMI.

WHAT IS NEXT?

The ongoing randomized controlled EURO-ICE study will demonstrate whether selective intracoronary hypothermia will reduce infarct size and improve clinical outcome.

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FIGURES LEGENDS

Figure 1. Schematic overview of the instrumentation for selective intracoronary hypothermia. OTWB: over-the-wire balloon.

Figure 2. Schematic overview of the occlusion phase (A) with inflated OTWB and saline infusion at room temperature (±22º C) and the reperfusion phase (B) with deflated OTWB and saline infusion at ±3-4º C. OTWB over-the-wire balloon.

Figure 3. Recording from the EURO-ICE study with aortic pressure in red (Pa), distal coronary pressure (Pd) in green and intracoronary temperature in blue. Note that during the reperfusion phase, the Pd rises (because the balloon is deflated) and coronary flow is (partially) restored. Numerical values of aortic, distal coronary pressure and temperature during both phases are displayed on the right of the screen.

Figure 4. Boxplots of the mean arterial pressure in mmHg and heart rate in beats per minute (bpm) before selective intracoronary hypothermia, during the occlusion phase, and during the reperfusion phase. * p=0.000; ** p=0.028; *** p=0.042; NS not significant.

Central Illustration: In-Hospital Safety Endpoints

	Selective intracoronary hypothermia during PPCI (N=50)	Standard PPCI (N=50)	P-value
Age, years (IQR)	62.1 (53.7 – 68.9)	64.9 (51.4 – 71.9)	0.73
Gender, n (%) - male - female	 45 (90) 5 (10)	 41 (82) 9 (18)	0.25
Medical history			
- Hypertension, n (%)	12 (24)	19 (38)	0.15
- Current smoking, n (%)	16 (32)	15 (30)	0.88
- Diabetes Mellitus, n (%)	4 (8)	7 (14)	0.34
- Hypercholesterolemia, n (%)	13 (26)	15 (30)	0.66
- Family history of CVD, n (%)	8 (16)	20 (40)	0.007
- Prior myocardial infarction, n (%)	2 (4)	0 (0)	0.50
- Prior PCI, n (%)	3 (6)	2 (4)	>0.99
Body temperature before procedure, ^{o} C (IQR)	36.2 (35.7 – 36.7)	36.1 (35.4 – 36.8)	0.81
Anterior wall STEMI			
- ∑ ST-deviation, mm (IQR)	16 (10 – 23)	13 (8 – 23)	0.26
Culprit occlusion - proximal LAD, n (%) - mid LAD, n (%)	 30 (60) 20 (40)	 26 (52) 24 (48)	0.42
Pre-PCI TIMI grade flow, n (%) - 0 - 1	 42 (84) 8 (16)	 45 (90) 5 (10)	0.37
Symptom onset-to-balloon time*, hh:mm (IQR)	2:23 (1:43 – 3:22)	2:44 (2:00 – 3:37)	0.03
Door-to-balloon time*, min (IQR)	30 (26 – 35)	24 (21 – 26)	<0.001

*Table 1. Baseline characteristics. * In the experimental arm (Selective intracoronary hypothermia during PPCI), symptom onset-to-balloon time and door-to balloon time exclude the duration of the occlusion phase.*

	Selective intracoronary hypothermia during PPCI (N=50)
Hypothermia – *Occlusion phase*	
- Time to target temperature, sec (IQR)	104 (17 – 165)
- Duration of occlusion phase, min (IQR)	8.00 (7.00 – 10.00)
- Δ intracoronary temperature*, ºC (IQR)	-6.47 (-6.00 – -7.00)
- Δ body temperature[§], ºC (IQR)	-0.20 (0.00 – -0.60)
- Rate of infusion, mL/min (IQR)	20 (20 – 22)
- Infused volume of saline, mL (IQR)	162.5 (132.5 – 200.0)
- Sustained VT or VF[#], n (%)	2 (4)
Hypothermia – *Reperfusion phase*	
- Duration of reperfusion phase, min (IQR)	10.00 (9.00 – 10.00)
- Δ intracoronary temperature*, ºC (IQR)	-6.44 (-5.29 – -7.59)
- Δ body temperature[§], ºC (IQR)	-0.10 (0.10 – -0.70)
- Rate of infusion, mL/min (IQR)	17 (14 – 20)
- Infused volume of saline, mL (IQR)	147.0 (128.0 – 205.0)
- Sustained VT or VF[#], n (%)	1 (2)

*Table 2. Procedural Data. *As a difference to baseline coronary temperature [§]As a difference to body temperature at arrival in catheterization laboratory [#]Necessitating for administration of anti-arrhythmic drugs and/or defibrillation.*

	Selective intracoronary hypothermia during PPCI (N=50)	Standard PPCI (N=50)	P-value
Rhythm disturbances			
- Atrial fibrillation, n (%)	0 (0)	1 (2)	>0.99
- Ventricular fibrillation*, n (%)	5 (10)	3 (6)	0.72
○ During hypothermia protocol, n (%)	3 (6)	-	
Onset of acute heart failure[§], n (%)	0 (0)	0 (0)	-
Post-PCI TIMI grade flow			0.08
- 0 or 1, n (%)	0 (0)	3 (6)	
- 2 or 3, n (%)	50 (100)	47 (94)	

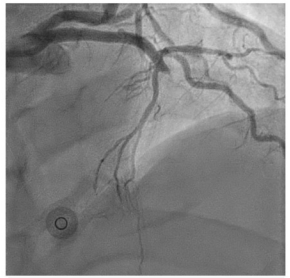
*Table 3A. Procedural safety endpoints. *Necessitating for administration of anti-arrhythmic drugs and/or defibrillation. [§]Definition for heart failure is use of intravenous diuretics, vasopressive agents or inotropics and/or left ventricular assist devices.*

	Selective intracoronary hypothermia during PPCI (N=50)	Standard PPCI (N=50)	P-value
Duration of hospitalization, days (IQR)	4 (4 – 5)	4 (3 – 5)	0.37
Rhythm disturbances			
- Atrial fibrillation, n (%)	0 (0)	2 (4)	0.50
- Ventricular fibrillation, n (%)	0 (0)	0 (0)	-
Stent thrombosis			
- Acute (<24 hours)	1 (2)	0 (0)	>0.99
- Subacute (24 hours to <30 days)	1 (2)	0 (0)	>0.99
Onset of acute heart failure[§], n (%)	1 (2)	1 (2)	>0.99
In-hospital mortality, n (%)	0 (0)	0 (0)	-

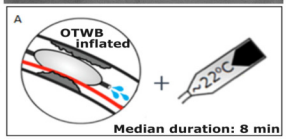
Table 3B. Safety endpoints during hospital admission after the index procedure. [§] Definition for heart failure is use of intravenous diuretics, vasopressive agents or inotropics and/or left ventricular assist devices.

IN-HOSPITAL SAFETY ENDPOINTS

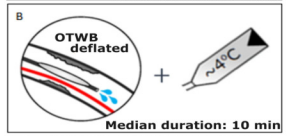
Selective intracoronary hypothermia during primary PCI (n=50)

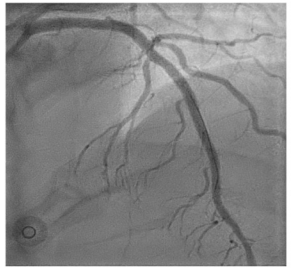


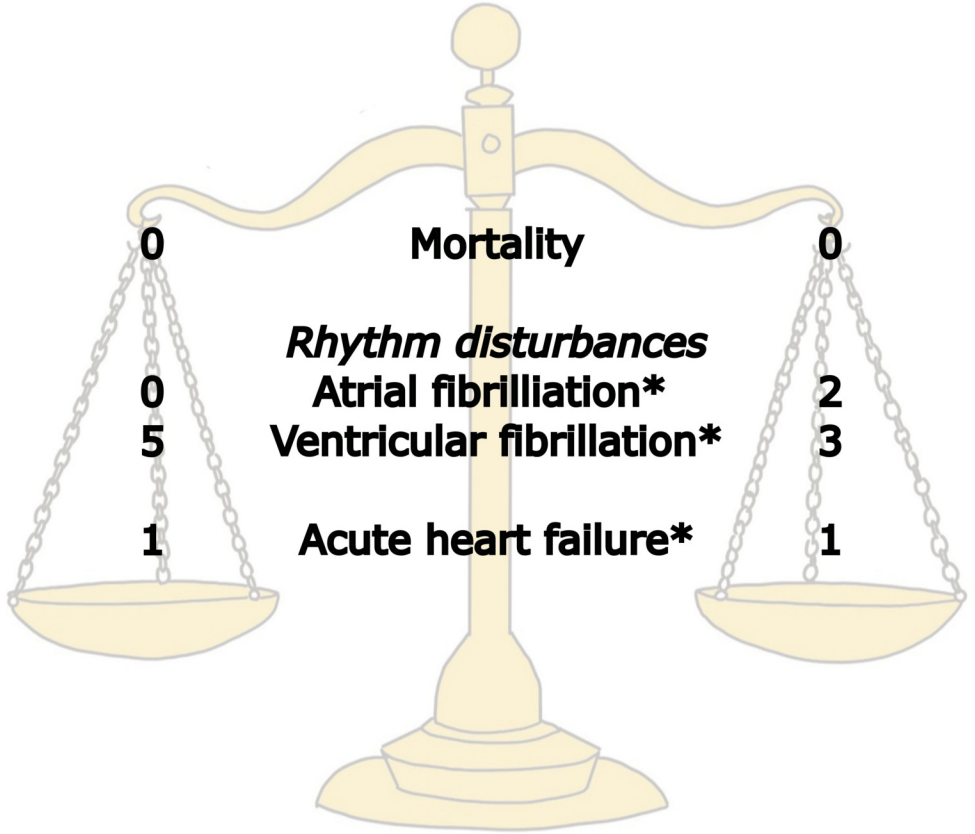
Occlusion phase



Reperfusion phase



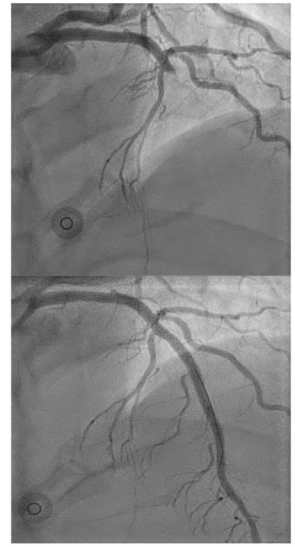




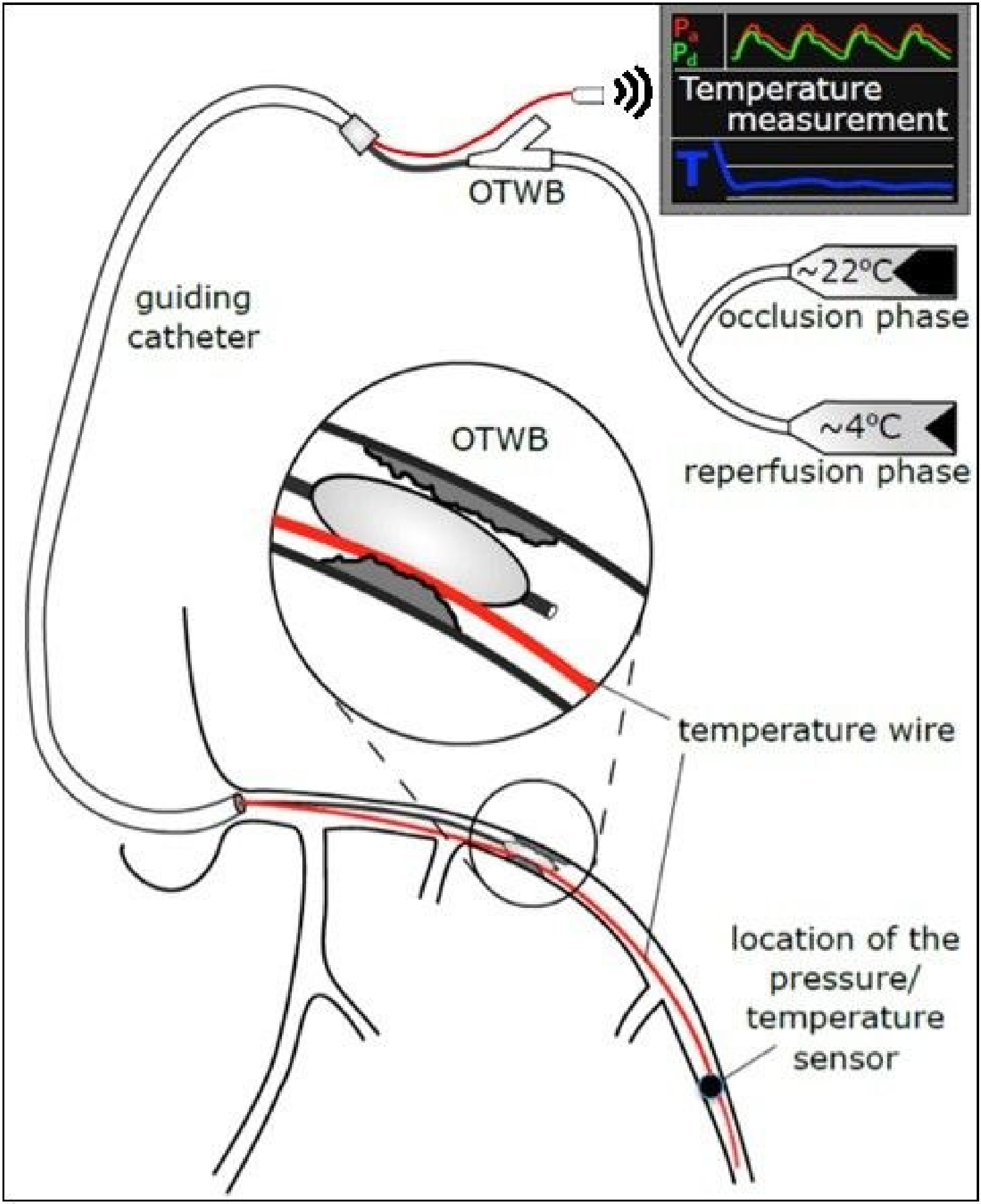
0	Mortality	0
	Rhythm disturbances	
0	Atrial fibrilliation*	2
5	Ventricular fibrillation*	3
1	Acute heart failure*	1

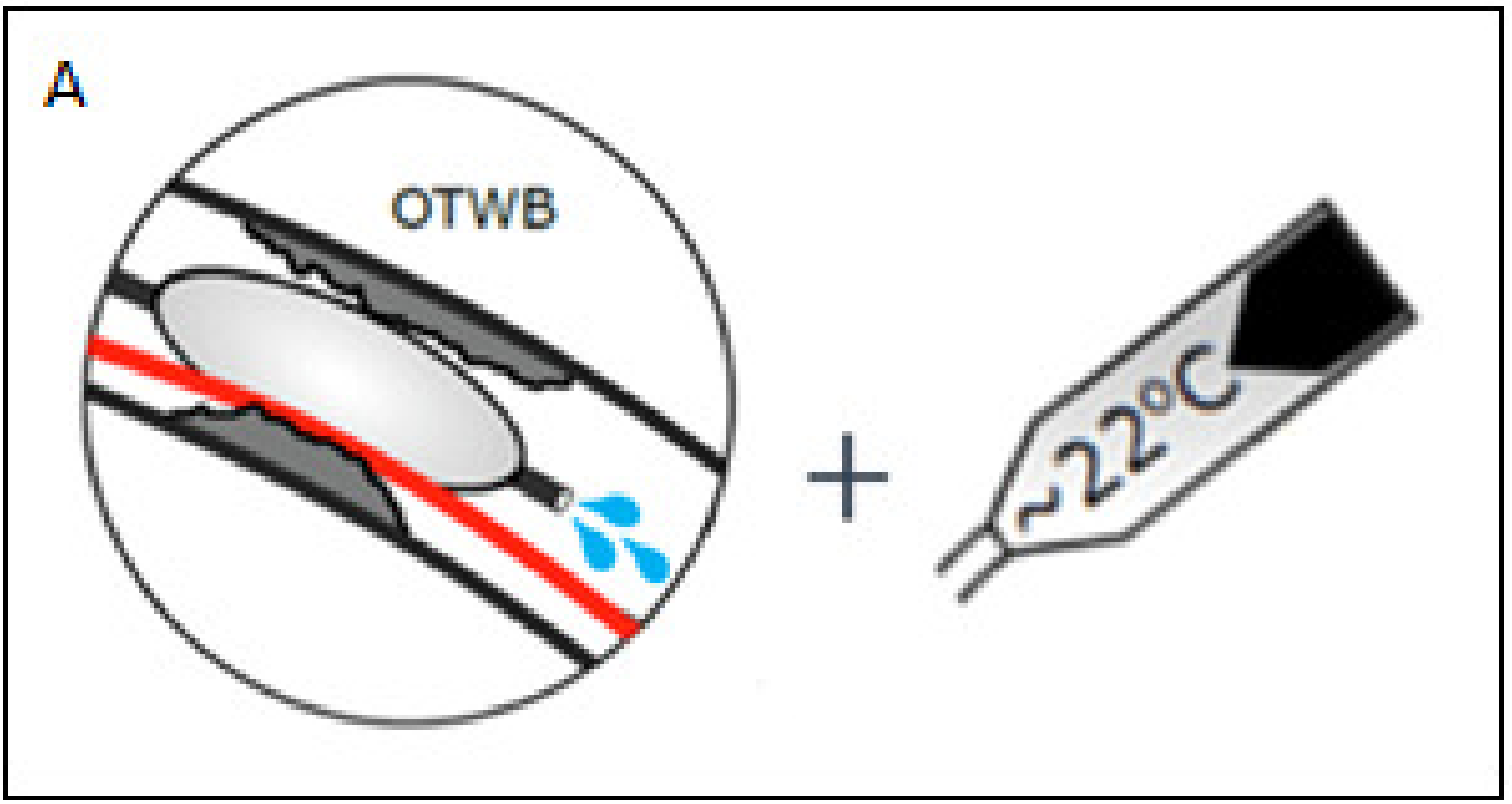
Primary PCI

(n=50)

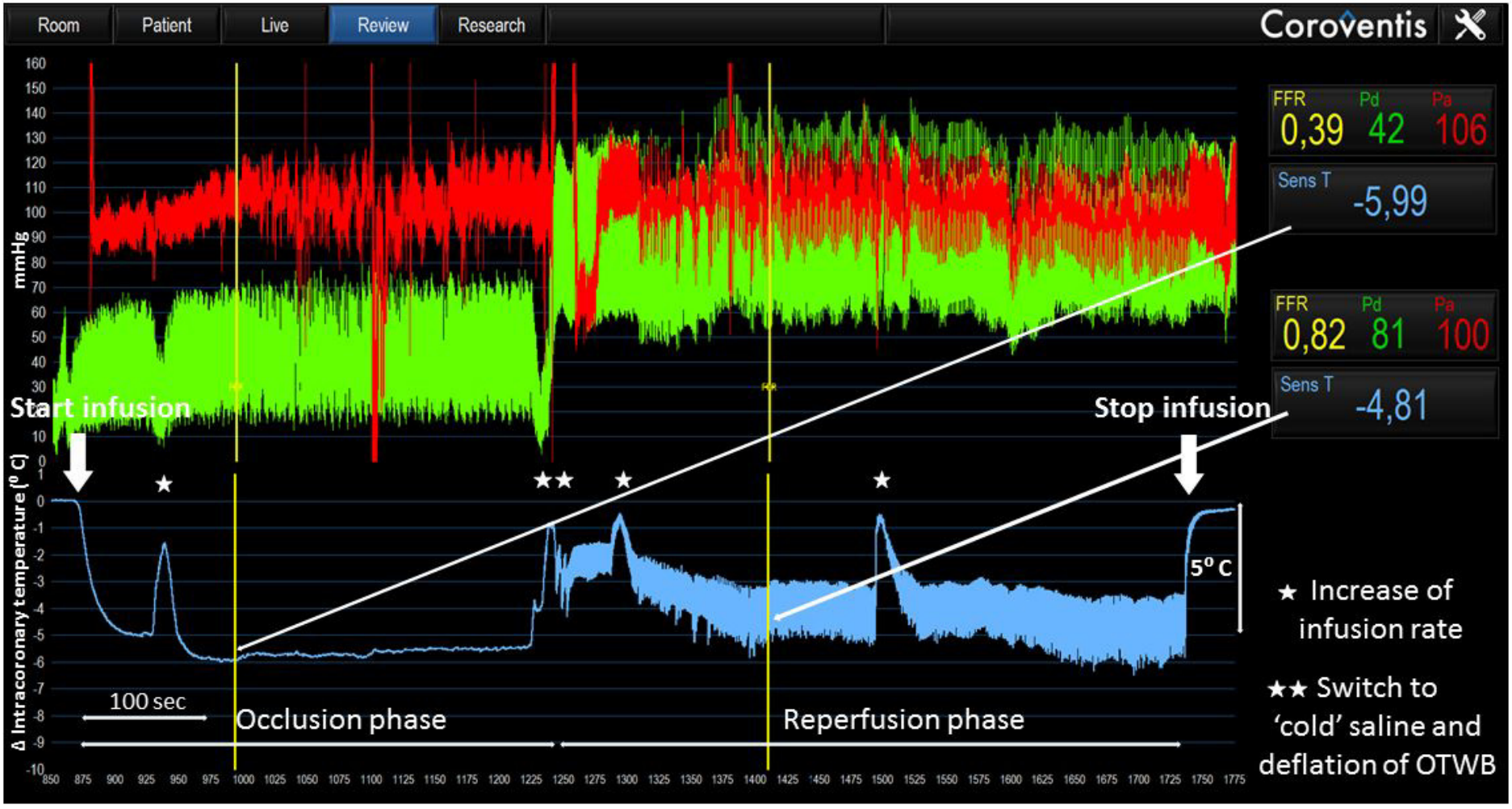


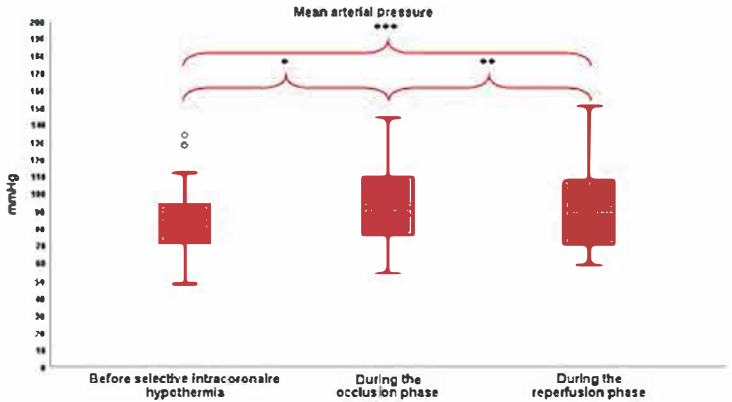
*non significant

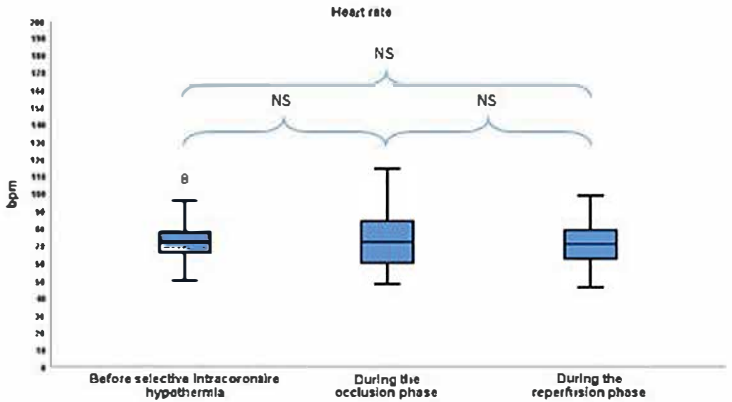

Temperature measurement
OTWB
guiding catheter
~22°C
occlusion phase
~4°C
reperfusion phase
OTWB
temperature wire
location of the pressure/ temperature sensor


A
OTWB
~22°C

B


Room
Patient
Live
Review
Research
Coroventis
FFR 0,39 Pd 42 Pa 106
Sens T -5,99
FFR 0,82 Pd 81 Pa 100
Sens T -4,81
mmHg
Start infusion
Stop infusion
Δ Intracoronary temperature (° C)
5° C
100 sec
Occlusion phase
Reperfusion phase
★ Increase of infusion rate
★★ Switch to 'cold' saline and deflation of OTWB


Mean arterial pressure
***
*
**
mmHg
Before selective intracoronaire hypothermia
During the occlusion phase
During the reperfusion phase


Heart rate
NS
NS
NS
bpm
Before selective intracoronaire hypothermia
During the occlusion phase
During the reperfusion phase