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ORIGINAL RESEARCH

EMERGING TECHNOLOGIES AND INNOVATIONS

Detection of Ischemic ST-Segment Changes Using a Novel Handheld ECG Device in a Porcine Model

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ABSTRACT

BACKGROUND Portable, smartphone-sized electrocardiography (ECG) has the potential to reduce time to treatment for patients suffering acute cardiac ischemia, thereby lowering the morbidity and mortality. In the UMC Utrecht, a portable, smartphone-sized, multi-lead precordial ECG recording device (miniECG 1.0, UMC Utrecht) was developed.

OBJECTIVES The purpose of this study was to investigate the ability of the miniECG to capture ischemic ECG changes in a porcine coronary occlusion model.

METHODS In 8 animals, antero-septal myocardial infarction was induced by 75-minute occlusion of the left anterior descending artery, after the first or second diagonal. MiniECG and 12-lead ECG recordings were acquired simultaneously before, during and after coronary artery occlusion and ST-segment deviation was evaluated.

RESULTS During the complete occlusion and reperfusion period, miniECG showed large ST-segment deviation in comparison to 12-lead ECG. MiniECG ST-segment deviation was observed within 1 minute for most animals. The miniECG was positive for ischemia (ie, ST-segment deviation ≥1 mm) for 99.7% (Q1-Q3: 99.6%-99.9%) of the occlusion time, while the 12-lead was only positive for 79.8% (Q1-Q3: 81.1%-98.7%) of the time ($P = 0.018$). ST-segment deviation reached maxima of 10.5 mm [95% CI: 6.5-14.5 mm] vs 5.0 mm [95% CI: 2.0-8.0 mm] for the miniECG vs 12-lead ECG, respectively.

CONCLUSIONS MiniECG ST-segment deviation was observed early and was of large magnitude during 75 minutes of porcine transmural antero-septal infarction. The miniECG was positive for ischemia for the complete occlusion period. These findings demonstrate the potential of the miniECG in the detection of cardiac ischemia. Although clinical research is required, data suggests that the miniECG is a promising tool for the detection of cardiac ischemia. (JACC Adv 2023;2:100410) © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ABBREVIATIONS AND ACRONYMS

AMI = acute myocardial infarction

CAG = coronary angiography

ECG = electrocardiogram

LAD = left anterior descending artery

STEMI = ST-segment elevation myocardial infarction

VF = ventricular fibrillation

VT = ventricular tachycardia

WCT = Wilson's central terminal

The electrocardiogram (ECG) is a crucial modality in the diagnosis of acute cardiac disease. The life-threatening nature of various cardiac disorders such as myocardial ischemia requires rapid and accurate ECG interpretation and accordant treatment. For patients suffering myocardial ischemia, pre-hospital ECG acquisition has shown to significantly decrease time-to-treatment, lowering the morbidity and mortality.[1-3]

To improve time-to-treatment, the ECG can be acquired in pre-hospital professional settings by general practitioners or by emergency staff, or for example by the patient at home. The latter poses the need for portable and small ECG devices, easily accessible to patients at any time and straightforward to operate without the need for a healthcare professional. Recently, many portable and small ECG devices have been investigated for this purpose.[4] While evidence shows high sensitivities regarding the detection of rhythm disorders, no currently available portable ECG devices have yet shown high accuracy in the detection of cardiac ischemia.[4,5]

Recently at the UMC Utrecht, we developed a portable and smartphone-sized device for ECG acquisition with 4 precordial electrodes to obtain a multi-lead ECG, the miniECG. The device is portable and reusable as it incorporates sustainable dry electrodes instead of disposable gel electrodes or patches. The miniECG is operated using a mobile app, which after short instructions can be used without the need for additional professional equipment or a healthcare professional. This study aims to investigate the ability of the miniECG to capture ischemia induced ST-segment changes during onset, presence and following acute coronary artery occlusion through comparison with 12-lead ECG in a porcine model.

METHODS

ANIMALS. Eight female Topigs Norsvin pigs with a median weight of 65.0 kg [IQR: 63.0-66.5 kg], were included in this research. All measurements were performed in addition to an ongoing project under project number (AVD1150020172624) authorized by the Animal Welfare Body in compliance with the Guide for the Care and Use of Laboratory Animals.[6] Sample size and animal sex were established not for this pilot study, but for the main project.

ANESTHESIA PROTOCOL. Starting 10 days before the experiment, the animals were given daily doses of clopidogrel (75 mg) and amiodarone (800 mg, first dose 1,200 mg). Acetylsalicylic acid (320 mg) was administered 1 day before the experiment. On the day of the experiment, the animals were premedicated with a single dose of ketamine (10 mg/kg), midazolam (0.5 mg/kg), atropine (0.05 mg/kg) and carprofen (2-3 mg/kg) i.m. General anesthesia was induced with a single dose of thiopental (4 mg/kg) i.v. and maintained by continuous i.v. administration of cisatracurium (0.7 mg/kg/h), midazolam (0.4 mg/kg/h) and sufentanil (2.5 μg/kg/h). After induction of general anesthesia, 300 mg of amiodarone was infused during 45 minutes.

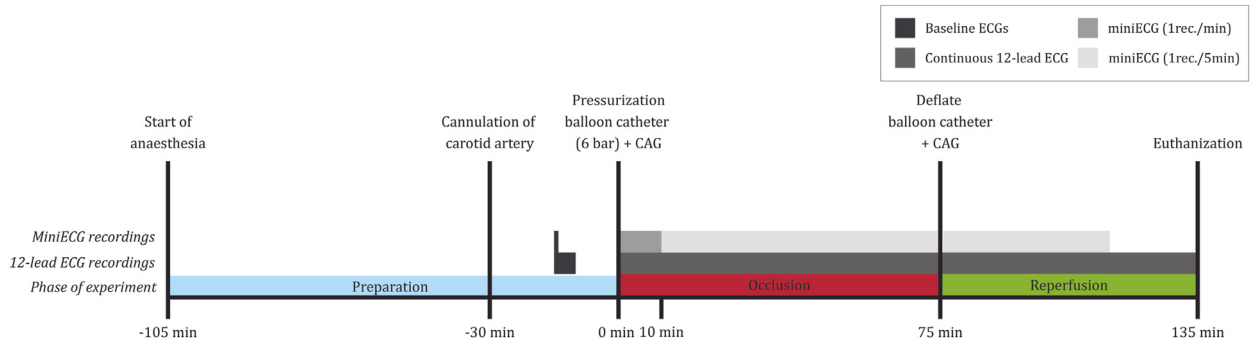
The animals were mechanically ventilated with a positive pressure ventilator, using a mix of oxygen and air (FiO_2 0.5), at a respiratory rate of 12/min and a tidal volume of 10 mg/kg. The positive end-expiratory pressure was adjusted between 2 cm and 3 cm H_2O to maintain an end-tidal CO_2 pressure between 35 mm Hg and 45 mm Hg. Body temperature was maintained between 36.5 °C and 38 °C with heating pads.

Heparin (15,000 IE) was given prior to cannulation of the carotid artery, prior to balloon occlusion and prior to reperfusion for anticoagulation. Blood pressure was monitored continuously by an arterial pressure catheter inserted in a peripheral artery.

OCCLUSION AND REPERFUSION. With the animal in supine position, the carotid artery and jugular vein were cannulated using 8-F sheaths. Coronary angiography (CAG) was performed to map the anatomy of the left anterior descending artery (LAD). A 3.0 mm balloon catheter (Sapphire II Pro, Orbus-Neich) was positioned after the first or second diagonal branch depending on coronary artery anatomy to induce sufficient ischemia while minimizing the risk of death due to refractory ventricular fibrillation (VF) during the experiment. The balloon catheter was pressurized to 6 bar to induce occlusion, after which successful occlusion was confirmed through CAG. After 75 minutes of occlusion the catheter was removed and reperfusion occurred during 60 minutes (**Figure 1**). The animals were euthanized after 60 minutes of reperfusion by administration of KCl (1,500 mg).

RESUSCITATION PROTOCOL. In case of hemodynamically intolerable arrhythmias, ie, VF and sustained ventricular tachycardia (VT), 200 J shocks were applied using the external paddles of a Heartstart XL defibrillator (Phillips, the Netherlands) alternated with manual chest compressions if needed. A dose of amiodarone (150 mg) was administered during every episode, with a maximum of 3 administrations.

FIGURE 1 Overview of the Experimental Protocol



miniECG and 12-lead ECG recordings were acquired before, during and after 75 minutes of coronary artery occlusion.

ECG RECORDINGS. For this experiment a prototype version of the miniECG (miniECG 1.0, UMC Utrecht) was used. The miniECG device uses 4 precordial stainless-steel electrodes to record 8 independent leads, at a sample frequency of 250 Hz for 10 seconds (**Figure 2**). Leads A1, L1, I1 and I2 of the miniECG are measured using electrode pairs (**Figure 2**). S1, A2, I3 and L2 of the miniECG are measured using the average of the other 3 electrodes as a reference. Electrode gel (Signa Gel, Parker) was applied to the miniECG electrodes for optimal electrical conduction. To obtain miniECG recordings, the miniECG device was positioned in the sternal midline of the animals, where the chest wall is flat to ensure skin contact of all 4 electrodes (**Central Illustration A**). 12-lead ECG electrodes were positioned according to standard clinical care, whilst keeping the central chest free for the miniECG and defibrillation (**Central Illustration A**).

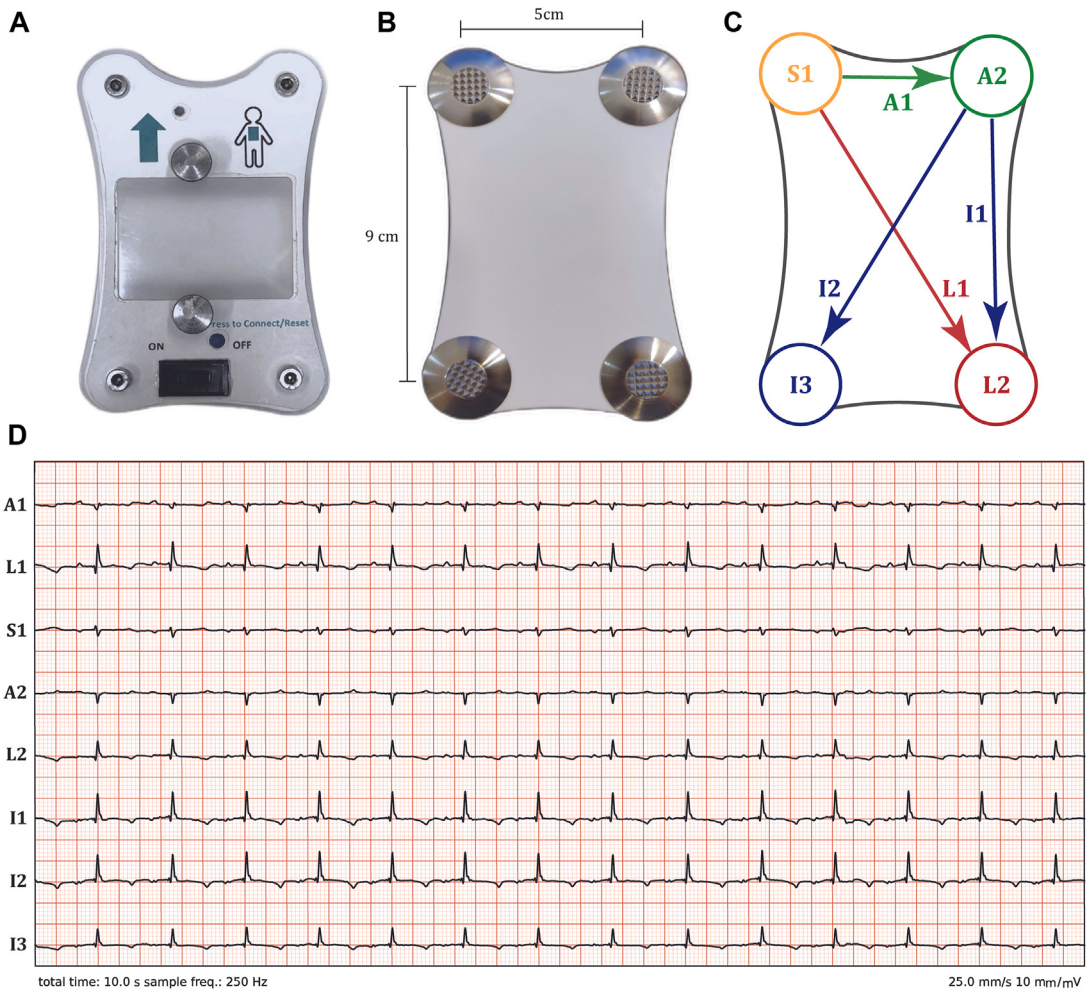
For each animal, three 10-second baseline miniECG recordings were acquired 5 minutes before occlusion. During occlusion, recordings were performed at interval of 1 minute for the first 10 minutes of occlusion and at an interval of 5 minutes for the rest of the experiment (**Figure 1**). Recordings were only performed if they did not interfere with essential steps of the rest of the experimental protocol, such as the administration of defibrillation shocks. MiniECG recordings were filtered bidirectionally using a digital third order bandpass Butterworth filter with cut-off frequencies of 0.67 Hz and 40 Hz, respectively. For comparison, 12-lead ECG recordings, sampled at 1,200 Hz and filtered to a bandwidth of 0.05 to 1,200 Hz were acquired simultaneously using the Cardioperfect PRO ECG Recorder (Welch Allyn).

ASSESSMENT OF ECGs. ST-segment deviation, defined as ST-segment elevation or reciprocal ST-segment depression, was measured at the J-point.[7] This was done for all leads of all miniECG recordings and at corresponding timepoints on the 12-lead ECGs. Measurements within 5 minutes after defibrillation shocks were excluded from analysis. Baseline QRS-amplitude (R-S) and T-wave amplitude were measured for both the miniECG and 12-lead ECG before occlusion.

STATISTICAL ANALYSIS. Median (IQR, Q1, Q3) were calculated for the baseline characteristics. For each animal, the miniECG lead and 12-lead ECG lead showing the largest ST-segment deviation were identified. For these leads, ST-segment deviation trendlines were fitted using MATLAB's (Version R2020b, MATLAB, The Math Works, Inc) smoothing spline fit for the occlusion period and reperfusion period separately. The smoothing parameter p was set to 0.05 to minimize noise in the trendlines. Weights w_i were set to 1, except for the pre-occlusion baseline measurement ($w_1 = 10$) to ensure the curve to fit this baseline ST-segment deviation value. For both the miniECG and the 12-lead ECG it was determined for what percentage of time of the 75-minute occlusion period the ECG showed ST-segment deviation ≥1 mm.

Additionally, mean and 95% CI of ST-segment deviation were evaluated over all pigs using the trendlines for the miniECG and the 12-lead ECG separately. Paired T-tests were used to assess

FIGURE 2 The miniECG Device and a Porcine Recording



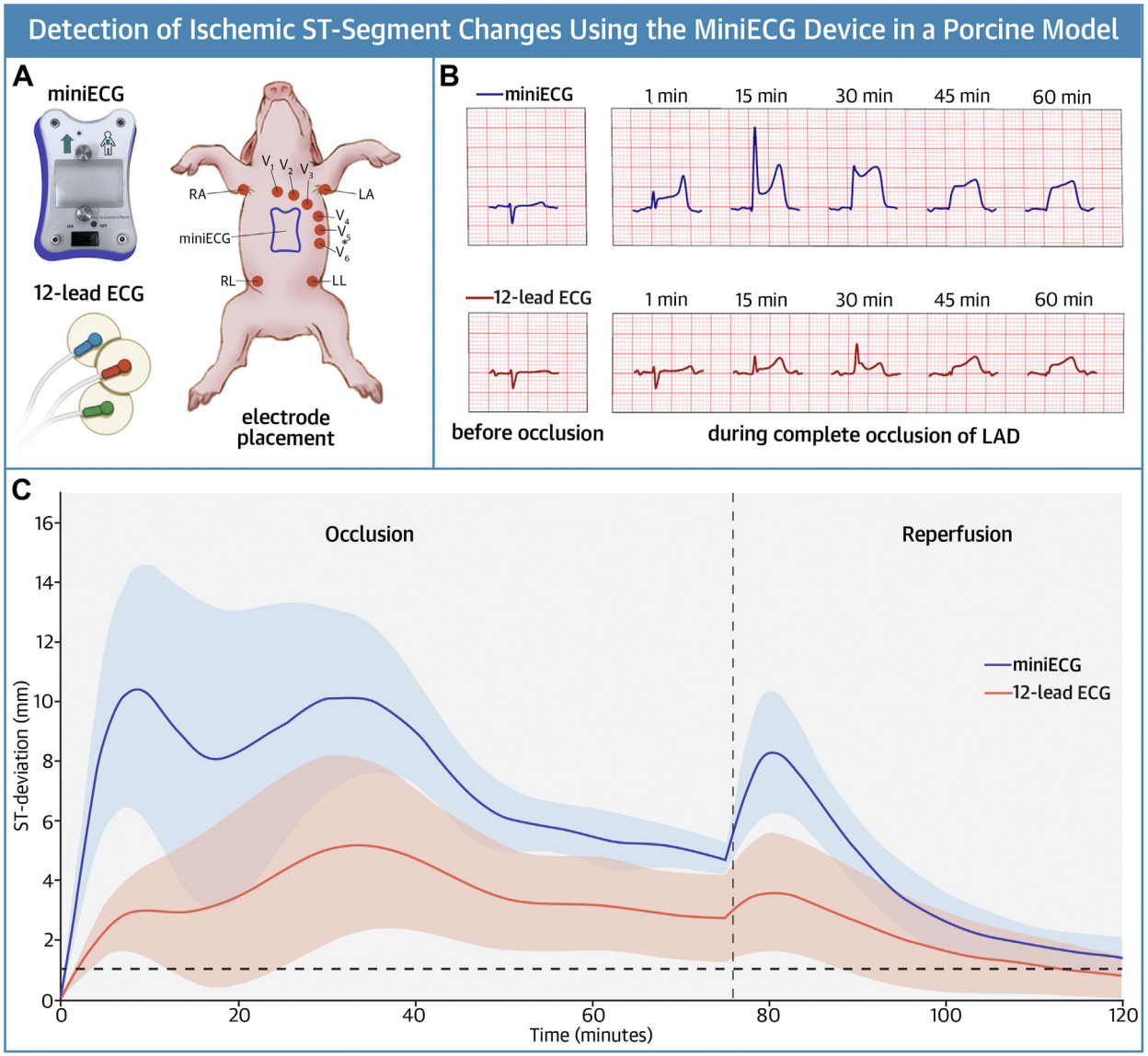
(A) Top side view of miniECG device. **(B)** Backside view of the miniECG with the 4 electrodes with spikes for optimal skin contact. **(C)** The 8 independent leads of the miniECG (A1, L1, S1, A2, L2, I1, I2, I3), as viewed from the frontal plane. **Arrows** indicate leads measured between electrode pairs. S1, A2, I3 and L2 are measured in reference to the Wilson Central Terminal (WCT), calculated as the average of the 3 remaining electrodes. **(D)** Example of a porcine miniECG recording.

differences between the miniECG and 12-lead ECG, regarding QRS amplitude at baseline and ST-segment deviation at peak ST-segment deviation at set timepoints. The Wilcoxon signed-rank test was used to evaluate the difference between mean percentage positive miniECG and mean percentage positive 12-lead ECG.

RESULTS

All 8 animals underwent the protocolized occlusion and reperfusion periods. Angiography showed complete occlusion of the LAD after inflation of the balloon catheter in all animals (Supplemental Figure 1) and return of the blood flow after deflation of the balloon catheter. During the occlusion period, the animals received a median of 22 (Q1-Q3: 8-36) defibrillation shocks for arrhythmias (**Table 1**). In 98% of miniECG recordings, no disturbing baseline wander or high frequency noise was observed and accurate assessment of morphology of the ST-segments was possible. In animals 1 and 3, no miniECG recordings were acquired in the first 30 minutes of occlusion due to technical failures. Apart from this, miniECG recordings could most often be performed at pre-specified timepoints

CENTRAL ILLUSTRATION **Detection of Ischemic ST-segment Changes Using the miniECG Device in a Porcine Model**



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(A) Positioning of miniECG and 12-lead ECG electrodes. **(B)** Changes in ST-segment in 1 animal at 15-minute intervals during occlusion in leads selected based on similar morphology (miniECG lead L1 and 12-lead ECG lead V_1). **(C)** Mean ST-segment deviation and 95% CI of the most deviated leads of the miniECG and 12-lead ECG during the occlusion period and reperfusion period. The horizontal dashed line shows a 1 mm threshold for ST-segment deviation. The vertical dashed line indicates the start of the reperfusion period at 75 minutes.

(Supplemental Figure 2). In animal 4 the 12-lead ECG recordings failed between 20 and 45 minutes of occlusion.

DIFFERENCES IN ST-SEGMENT DEVIATION MAGNITUDE. QRS-amplitude and T-wave amplitude did not significantly differ between miniECG and 12-lead ECG at baseline, before occlusion ($P = 0.609$, $P = 0.191$, respectively) (Supplemental Table 1). ST-segment deviation measured at the J-point was <1 mm for all animals before occlusion for both the miniECG and 12-lead ECG.

Both the miniECG and 12-lead ECGs showed ST-segment deviation of large magnitude from the early occlusion period onwards (**Central Illustration B**

TABLE 1 Animal Characteristics

	Animal								
	1	2	3	4	5	6	7	8	Median (IQR)
Demographics									
Weight (kg)	67.0	66.0	67.5	66.5	64.0	63.5	57.0	60.5	65.0 (63.0-66.5)
Events									
Episodes of hemodynamically intolerable arrhythmia during occlusion	3	0	9	3	7	3	2	2	3 (2-4)
Defibrillation shocks	9	0	30	75	54	25	6	18	22 (8, 36)
Time to first defibrillation shock (min)	18.0	-	4.6	4.0	16.5	17.6	16.7	15.5	16.5 (10.1-17.2)
Chest compression sessions	0	0	0	3	3	2	0	1	1 (0-2)
Amiodarone administered during experiment (mg)	450	0	450	450	450	450	300	300	450 (300-450)
Dopamine administered IV (start time in min)	-	-	30	32	38	32	-	-	32 (31.5-33.5)

Demographics of the 8 female Topigs Norsvin pigs included in the experiment and cardiac events that occurred during the experiment.

and C). Maximal ST-deviation was observed in leads L1 (62.5%), I2 (25%) and A1 (12.5%) for the miniECG and in leads V_3 (37.5%), V_4 (37.5%) and V_2 (25%) for the 12 lead-ECG. The miniECG was positive for ischemia (ie, ST-segment deviation ≥1 mm) for 99.7% of the occlusion time, while the 12-lead was only positive for 79.8% of the time ($P = 0.018$) (Supplemental Figure 3). Mean miniECG ST-segment deviation was of significantly larger magnitude compared to 12-lead ECG ST-segment deviation during the complete occlusion period (**Central Illustration C**).

The miniECG was positive for ischemia earlier than the 12-lead ECG in all animals. At 1 minute, 4 of 8 animals had both a successful miniECG recording and a 12-lead ECG recording. In 3 of 8 of these animals ST-segment deviation ≥1 mm was observed on the miniECG, compared to 1 animal with ST-segment deviation ≥1 mm on the 12-lead ECG. At the timepoint of 2 minutes after occlusion, the combination of a miniECG and a 12-lead ECG recording was available in 5/8 animals. All 5 showed ST-segment deviation ≥1 mm on the miniECG vs 3 on the 12-lead ECG. At the timepoint of 5 minutes of occlusion, ST-segment deviation ≥1 mm was visible for all miniECG and 12-lead ECG recordings in 5 animals with available data at that timepoint.

ST-DEVIATION PEAKS. While maximum ST-segment deviation differed, miniECG ST-segment deviation and 12-lead ST-segment deviation showed similar trends during occlusion and reperfusion. In general, 2 peaks in ST-segment deviation were observed during occlusion. The miniECG showed local maxima of 10.5 mm (95% CI: 6.5-14.5 mm) at 8 minutes of occlusion and 10.0 mm (95% CI: 7.0-13.0 mm) at 33 minutes of occlusion. For the 12-lead ECG these local maxima were 3 mm [95% CI: 1.5-4.5 mm] at 10 minutes of occlusion and 5.0 mm (95% CI: 2.0-8.0 mm) at 33 minutes of occlusion. After the second peak, ST-segment deviation decreased for both the miniECG and 12-lead ECG. During reperfusion, a sudden increase of ST-segment deviation was observed, miniECG and 12-lead ECGs reached maximum ST-segment deviation of 8.0 mm [95% CI: 6.0-10.0 mm] and 3.5 [95% CI: 1.5-5.5 mm], respectively, after 5 minutes of reperfusion, after which ST-segment deviation decreased. In the 40 minutes after reperfusion, ST-segment deviation did not yet reach baseline values.

DISCUSSION

In this study, we investigated the ability of the miniECG to capture ischemia induced ST-segment changes during onset, presence and following coronary artery occlusion through comparison with the standard 12-lead ECG in a porcine model of myocardial infarction. The miniECG was able to detect ischemic ST-segment deviation within 1 minute. Detection of cardiac ischemia is especially relevant in the early phase, to prevent ischemia induced sudden cardiac arrest, a major cause of death worldwide.[8] More importantly, the miniECG was positive for 99.7% (Q1-Q3: 99.6%-99.9%) of the occlusion period in all animals, while the 12-lead ECG was only positive for 79.8% (Q1-Q3: 81.1%-98.7%) of this period. This suggests that the miniECG is a promising tool for the detection of cardiac ischemia in the pre-hospital and home setting, capturing ST-segment changes compared to the gold standard.

ST-SEGMENT DEVIATION PEAKS. Our results show 2 ST-segment deviation peaks between 10 and 40 minutes of occlusion after which ST-segment deviation

decreases (**Central Illustration C**). During reperfusion a short-lived increase in ST-segment deviation was observed after which the ST-segments normalized. This is in line with the dynamic changes of the ST-segment in porcine coronary artery occlusion as described in similar studies.[9-11] The short-term increase of ST-segment deviation during reperfusion is most likely caused by reperfusion injury of the myocardium.[9,12-14]

To the best of our knowledge, there have been no publications on the mechanisms behind the 2 separate peaks in ST-segment deviation during the first hour of coronary artery occlusion. Interestingly, the timepoints of the observed peaks correlate with incidence and different mechanisms of ventricular fibrillation (VF) during coronary artery occlusion as reported in a review by Diego et al.[15] More research is needed to investigate a possible relation between the incidence and mechanisms of VF and peaks in ST-segment deviation during coronary artery occlusion.

MiniECG DEVELOPMENT. Technical failure of the miniECG in the 2 animals was caused by shortcomings of the design of the prototype that was used for these experiments. These prototype versions were designed to investigate feasibility of the new 4-electrode measuring method, but not yet optimized for final use by patients. Experiences in both in the lab and in patient studies were used to optimize the design of the miniECG and these issues have been solved.

CLINICAL APPLICATION. Time delay between onset of symptoms and seeking medical attention is a major factor in mortality and morbidity in patients with acute myocardial infarction (AMI).[16] The miniECG was developed as a portable, smartphone sized ECG device for easy self-use by patients, in the future enabling the acquisition of an ECG within 1 minute.

We envision the following: Upon the onset of chest pain, a patient places the miniECG centrally on the chest, and starts a recording through an app on a paired smartphone. Ideally, the app would immediately be able to triage the recorded ECG, and advise the patient to take appropriate action. Alternatively, the recording could be send to a physician for evaluation.

Alternative uses of the miniECG could include (para)medical facilities where no 12-lead ECG is readily available, such as certain nursing homes or general practitioners' offices. The miniECG may decrease delay between onset of symptoms and seeking medical attention, possibly decrease mortality and morbidity of AMI, as hospitals can be alerted and can respond and prepare accordant treatment.[17-21]

The time-dependent character of ST-segment changes in cardiac ischemia emphasizes the added value of portable and smartphone sized ECG devices that can be used in the home setting.[22] A patient experiencing cardiac symptoms can record an ECG, allowing early diagnosis. On the other hand, in patients with persisting complaints, the miniECG poses opportunities for easy follow up through repetition of ECG in patients with initial non-diagnostic ECG until 12-lead ECG is available.

STUDY LIMITATIONS. A porcine model was used as it resembles the human heart as close as possible, especially regarding coronary anatomy. Nonetheless, the positioning of the porcine heart in relation to the chest is different compared to humans, as well as the anatomy of the conduction system and electrophysiological properties,[23,24] resulting in an abnormal ECG considering clinical conventions. Therefore, results of this study cannot be directly translated into human clinical setting.

The magnitude 12-lead ECG ST-segment deviation in this study is lower than reported in similar studies.[25,26] To keep the central chest free for the placement of defibrillation paddles, the 12-lead ECG electrodes were placed craniolaterally (**Central Illustration A**). As measured ST-segment deviations are strongly influenced by electrode position with respect to the ischemic area, this craniolateral placement of the precordial 12-lead electrodes is generally expected to result in ST-segment deviation of smaller magnitude.[27,28] This is both further away from the heart, and at a non-perpendicular angle in respect to the anteroseptal ischemia of the porcine heart. For this reason, ST-segment deviation amplitudes cannot be directly compared between the 12-lead ECG and miniECG.

Nonetheless, the high amplitudes of miniECG ST-segment deviation are striking. It is interesting to see these high amplitudes with a device that does not use a limb-electrode-based Wilson's Central Terminal (WCT), but a WCT that is calculated based on the precordial electrodes (**Figure 2**). Detection of large ST-deviations was possible with this less optimal WCT that is not truly centered.

The need for defibrillation shocks in case of hemodynamically intolerable ventricular arrhythmias influenced the study data in 2 ways. Firstly, as the device is handheld, it had to be removed during the appliance of defibrillation shocks, leading to data loss. Secondly, defibrillation shocks have a short-lived effect on the ST-segment, documented to occur shorter

than 5 minutes in most cases.[29-32] To eliminate the effect of these defibrillation shock-induced ST-segment deviation, measurements within 5 minutes of defibrillation shocks were excluded from the analysis. A more aggressive anti-arrhythmic treatment could have decreased the incidence of arrhythmias, but this was not possible as this study was performed as an extension of an ongoing study.

CONCLUSIONS

This study aims to investigate the capture of ischemic ST-segment changes by a new handheld precordial electrode recording device (miniECG). In a porcine model of transmural antero-septal cardiac ischemia, we have observed that: 1) the miniECG records high quality ECG showing ST-segment deviation; 2) miniECG ST-segment deviation was observed early and was of large magnitude during 75-minutes of coronary artery occlusion; and 3) the miniECG was positive for ischemia for 99.7% of the occlusion period. These findings demonstrate the potential of the miniECG as a portable smartphone-sized ECG device in the detection of cardiac ischemia. Diagnostic criteria and accuracy of the miniECG in relation to cardiac ischemia in humans with different anatomical areas need to be evaluated further in clinical research.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: The ECG is an essential tool in the diagnosis of cardiac ischemia. The results of this study show the potential of the miniECG to capture of ST-deviation during coronary artery occlusion in a porcine model.

TRANSLATIONAL OUTLOOK: Clinical studies comparing ECGs and miniECGs of patients without and with cardiac ischemia are needed to translate these animal study findings towards patients. For implementation of the miniECG in (pre)hospital care, miniECG specific diagnostic criteria for the detection of cardiac ischemia should be developed through clinical research.

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APPENDIX For supplemental figures and table, please see the online version of this paper.