Automated cardiac arrest detection using a photoplethysmography wristband: algorithm development and validation in patients with induced circulatory arrest in the DETECT-1 study

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Summary

Background Unwitnessed out-of-hospital cardiac arrest is associated with low survival chances because of the delayed activation of the emergency medical system in most cases. Automated cardiac arrest detection and alarming using biosensor technology would offer a potential solution to provide early help. We developed and validated an algorithm for automated circulatory arrest detection using wrist-derived photoplethysmography from patients with induced circulatory arrests.

Methods In this prospective multicentre study in three university medical centres in the Netherlands, adult patients (aged 18 years or older) in whom short-lasting circulatory arrest was induced as part of routine practice (transcatheter aortic valve implantation, defibrillation testing, or ventricular tachycardia induction) were eligible for inclusion. Exclusion criteria were a known bilateral significant subclavian artery stenosis or medical issues interfering with the wearing of the wristband. After providing informed consent, patients were equipped with a photoplethysmography wristband during the procedure. Invasive arterial blood pressure and electrocardiography were continuously monitored as the reference standard. Development of the photoplethysmography algorithm was based on three consecutive training cohorts. For each cohort, patients were consecutively enrolled. When a total of 50 patients with at least one event of circulatory arrest were enrolled, that cohort was closed. Validation was performed on the fourth set of included patients. The primary outcome was sensitivity for the detection of circulatory arrest.

Findings Of 306 patients enrolled between March 14, 2022, and April 21, 2023, 291 patients were included in the data analysis. In the development phase (n=205), the first training set yielded a sensitivity for circulatory arrest detection of 100% (95% CI 94–100) and four false positive alarms; the second training set yielded a sensitivity of 100% (94–100), with six false positive alarms; and the third training set yielded a sensitivity of 100% (94–100), with two false positive alarms. In the validation phase (n=86), the sensitivity for circulatory arrest detection was 98% (92–100) and 11 false positive circulatory arrest alarms. The positive predictive value was 90% (95% CI 82–94).

Interpretation The automated detection of induced circulatory arrests using wrist-derived photoplethysmography is feasible with good sensitivity and low false positives. These promising findings warrant further development of this wearable technology to enable automated cardiac arrest detection and alarming in a home setting.

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Introduction

Out-of-hospital cardiac arrest (OHCA) is a leading cause of global mortality.[1–3] The fast recognition of cardiac arrest and initiation of cardiopulmonary resuscitation are key to survival.[4,5] Over the past decade, survival to hospital discharge has improved to up to 23% and is probably related to the introduction of public access defibrillators and smartphone-activated volunteer responders.[1,2,6–8] However, for people with unwitnessed cardiac arrest (up to 50% of all patients with cardiac arrest), survival chances are poor (<5%), because the emergency medical chain is activated too late in most cases.[1,9,10]

Automated cardiac arrest detection and alarming might catalyse the early help for people with unwitnessed cardiac arrest and shorten treatment delays for people with witnessed cardiac arrest. Most people with OHCA were not identified as high risk before the event and were therefore not protected by implantable cardioverter defibrillators (ICDs).[11,12] Wearable biosensor technologies are widely used in the current era to monitor health status, both by consumers and as a part of remote patient monitoring.[13] If these become suitable to automatically detect and alarm in the case of cardiac arrest, this would allow earlier help and could improve OHCA survival chances.[14]

Research in context

Evidence before this study

We searched PubMed for research published in English between database inception and Aug 21, 2023, with search terms expressing cardiac or circulatory monitoring (eg, "automated detection", "wearable", "photoplethysmography", and "continuous monitoring") in combination with search terms comprising cardiac arrest (eg, "out-of-hospital cardiac arrest", "OHCA", "unwitnessed", and "early cardiopulmonary resuscitation"). In September, 2022, a systematic review was published, summarising the existing evidence on innovative biosensor technologies for early detection of out-of-hospital cardiac arrest (OHCA). Among the four included studies, three studies investigated wearable devices, of which one older study used mechanical plethysmography and two studies used electrocardiography as the main sensor technology. Results were obtained in small sample sizes and real-world data were absent. The other study used breathing sounds during sleeping to detect cardiac arrest. For photoplethysmography, the feasibility to detect haemodynamic instability has been shown in animal studies. In addition, photoplethysmography is proposed for the detection of a return of spontaneous pulses during heart rhythm checks during cardiopulmonary resuscitation.

Added value of this study

The DETECT programme is set up to develop a wearable wristband-based full technological solution for automated cardiac arrest detection and alarming in a home setting. DETECT-1 is a prospective multicentre study to develop and validate the photoplethysmography based circulatory arrest detection algorithm using patient data of induced circulatory arrests. Relying solely on photoplethysmography data, induced circulatory arrest was detected with excellent sensitivity and low false positives.

Implications of all the available evidence

Wearable biosensor technologies might offer a technological solution for automated cardiac arrest detection and alarming. If available, this potential breakthrough technology could markedly improve survival chances from unwitnessed OHCA. DETECT-1 is the first prospective study developing and validating a circulatory arrest detection algorithm in a large sample of patients with true circulatory arrests and with non-cardiac arrest data that includes fragments with noise and cardiac arrhythmias. The promising results warrant further development of this wearable technology to enable cardiac arrest detection in a home setting.

There are sparse data from proof-of-concept studies on the use of wearable biosensors for automated cardiac arrest detection, but no such wearable biosensor is available yet.[15] The studies had a small study population, and often used simulated data sets, without validation of their findings. Moreover, it is questionable whether the application of electrocardiographic (ECG) sensors is feasible for continuous long-term monitoring.[13] Photoplethysmography is a sensor technique that is used in smartwatches to monitor the heart rate at the wrist.[13] It is non-invasive, easy-to-use, affordable, and could detect circulatory arrest on the basis of the absence of pulsatile flow. Previous animal studies have shown the feasibility to detect haemodynamically unstable arrhythmias using photoplethysmography sensors.[16,17] On the basis of these data, we hypothesised that an algorithm using wrist-derived photoplethysmography could accurately detect circulatory arrest.

To enable automated cardiac arrest detection and activation of the emergency medical system, medical reliability is essential, with excellent sensitivity and low false positives. In the DETECT project, an existing wristband for remote monitoring is further developed to enable automated cardiac arrest detection and alarming during daily life using multiple sensor technologies including wrist-derived photoplethysmography. The present DETECT-1 study is a prospective multicentre study to develop and validate a photoplethysmography based algorithm for automated circulatory arrest detection in patients with induced circulatory arrest.

For the **study protocol** see www.detect-study.com/partners/participating-centers/

Methods

Study design and participants

DETECT-1 is a prospective multicentre study in adult patients (aged 18 years or older) in whom short-lasting circulatory arrest was induced as part of routine practice during transcatheter aortic valve implantation (TAVI), subcutaneous ICD (S-ICD) implantation, or ventricular tachycardia ablation. The exclusion criteria were a known bilateral significant subclavian artery stenosis or medical issues interfering with the wearing of the wristband. The study was conducted at three university medical centres in the Netherlands between March 14, 2022, and April 21, 2023, and was set up by research consortium DETECT consisting of Radboud University Medical Center (Nijmegen, the Netherlands), Erasmus MC Cardiovascular Institute, University Medical Center Rotterdam (Rotterdam, the Netherlands), Reinier de Graaf Hospital (Delft, the Netherlands), and Corsano Health (The Hague, the Netherlands). Consecutive patients who met the inclusion criteria were selected for the study. The study protocol was approved by the Medical Research Ethics Committee Netherlands East. Written informed consent was obtained from participants before inclusion.

Study procedures and data collection

Study participants were equipped with a wrist-worn photoplethysmography device (CardioWatch 287–2, Corsano Health, The Hague, the Netherlands) during the TAVI procedure, S-ICD implantation, or ventricular

tachycardia ablation. Before the start of the procedure, the wristband was applied. The wristband was worn on the left wrist; in cases where there was no space on the left side (related to the insertion of other lines—eg, the arterial line), the right wrist was used. Photoplethysmography data (multi-wavelength [paired green, red, and infrared sensors]; sample frequency 32 Hz or 128 Hz, whichever was available [all photoplethysmography data were down-sampled to 32 Hz before the data analysis]) were recorded during the entire procedure and sent by a Bluetooth-connected smartphone (Samsung Galaxy A40, Android OS, Samsung Electronics, Seoul, South Korea) to a protected cloud. As a reference standard, arterial blood pressure was monitored through the cannulation of a peripheral artery (radial or femoral artery) or by measuring central aortic pressure through the catheter, or both. Additionally, ECG data were continuously collected and stored (ICM+ software, University of Cambridge, Cambridge, UK, or Sensis software, Siemens Healthineers, Erlangen, Germany). Baseline variables, including age, sex, skin type (Fitzpatrick scale), and arm hair density, were collected.[18,19]

Event definition

Induced circulatory arrests were defined as follows. First, for TAVI procedures, induced circulatory arrests were defined as rapid ventricular pacing during aortic balloon inflation; this results in short-lasting circulatory standstill and is routinely performed during balloon-expandable valve placement, and balloon dilatation before or after the valve implantation (figure 1). In cases where balloon dilatation was not performed, patient data were used as non-circulatory arrest data. Second, for S-ICD procedures, induced circulatory arrests were defined as the induction of ventricular fibrillation using a 50 Hz alternating current burst for 4–10 s during defibrillation testing. And third, for ventricular tachycardia ablation, induced circulatory arrests were defined as the induction of haemodynamically unstable ventricular tachycardia (mean arterial pressure ≤45 mm Hg or absence of pulsatile flow [pulse pressure ≤15 mm Hg]) as established using invasive arterial blood pressure measurements.[20–22]

Event times were annotated during the procedures by the catheterisation laboratory personnel and confirmed by the assessment of ECG data afterwards (RE and JLB). All other photoplethysmography data where reference recordings were assessable, including data from patients without any circulatory arrest induction, were labelled as non-circulatory arrest data, except for periods of spontaneous haemodynamic instability, defined as invasive mean arterial pressure of 45 mm Hg or less, or the absence of pulsatile flow (pulse pressure ≤15 mm Hg).[20–22] These episodes consisted of TAVI procedure-related complications including severe haemodynamic instability or non-induced cardiac arrests, or were related to the inflation of the blood pressure cuff at the same arm as where the wristband was applied.

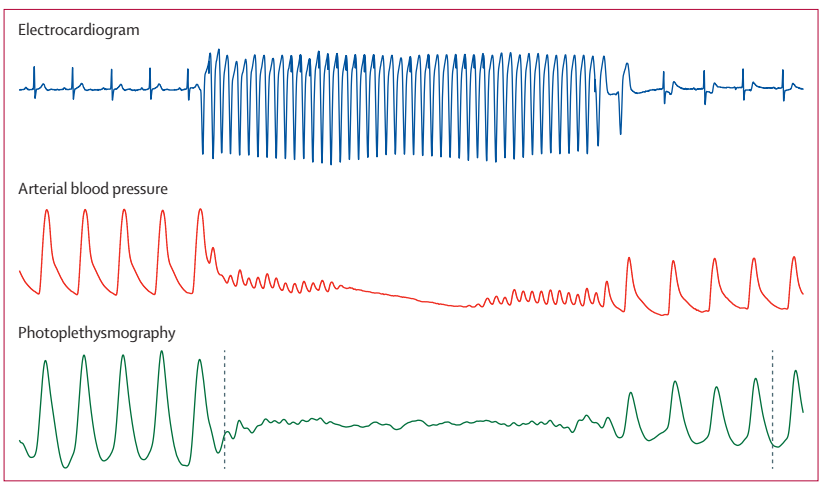

Figure 1: **Example of a circulatory arrest induction in a patient in the TAVI group**
Rapid ventricular pacing with aortic balloon inflation during TAVI resulted in a short-lasting circulatory arrest (total duration 14 s). The electrocardiogram signal is represented in blue, the invasively measured arterial blood pressure in red, and the photoplethysmography signal in green. The initial heart rhythm was a sinus rhythm with a baseline blood pressure of 130/50 mm Hg. After the initiation of rapid ventricular pacing, the blood pressure decreased, and during aortic balloon inflation (in the middle of the figure) there was no pulsatile flow. After aortic balloon deflation and the discontinuation of rapid ventricular pacing, the patient regained sinus rhythm, and the blood pressure returned to normal levels. The markings in the photoplethysmography signal indicate the moment of detection and termination of the circulatory arrest alarm generated by the developed algorithm.
TAVI=transcatheter aortic valve implantation.

Data processing and algorithm development

The photoplethysmography signals of the two green photoplethysmography channels were averaged and used for the development of the circulatory arrest detection algorithm based on photoplethysmography. The photoplethysmography algorithm was developed on the basis of three consecutive training cohorts to enable algorithm refinement. For each cohort, patients were consecutively enrolled. When a total of 50 patients with at least one event of circulatory arrest were enrolled, that cohort was closed. The fourth iteration was used as a final algorithm evaluation (labelled the validation phase; approximately a third of all events). For the final evaluation of the algorithm, no changes were made to the algorithm, and photoplethysmography and reference data were separately assessed—namely, the algorithm developer (KE) was masked to event annotations, blood pressure, and ECG data; and assessors of the reference data (RE and JLB) were masked to photoplethysmography data and circulatory arrest alarms.

The photoplethysmography signal was analysed as follows. First, a second-order Butterworth band-pass filter with a frequency range of 0·5–4·0 Hz was applied to remove low-frequency and high-frequency noise. Then, for every patient, the amplitude of the baseline photoplethysmography signal was established and used to define a patient-specific threshold for potential circulatory arrest. When the individual photoplethysmography peaks (corresponding to cardiac cycles) of the continuous photoplethysmography signal decreased below this threshold, these peaks were

assessed according to predefined signal quality criteria. This signal quality index consists of a combination of signal features that identify whether individual photoplethysmography peaks conform to the normal shape of a photoplethysmography wave.[23] A signal amplitude of less than the threshold combined with a poor signal quality index for 5 s or longer resulted in a circulatory arrest alarm. An alarm was terminated after the detection of a restoration of the pulsatile photoplethysmography signal. The assessment of circulatory arrest alarms was performed during post-processing. Between the consecutive iterations, amplitude thresholds and photoplethysmography quality criteria were adapted manually to improve algorithm performance. Additionally, the number of normal photoplethysmography peaks needed to be detected to terminate a circulatory arrest alarm was increased. A detailed description of the algorithm is provided in the appendix (pp 1–6). Data analyses were performed in Python (version 3.10).

See Online for appendix

Statistical analysis

Details regarding the power calculation can be found in the study protocol. Continuous baseline variables were presented as mean and SD or median and IQR, depending on the normality of the distribution (established using a Shapiro–Wilk test). Comparisons were made with a Student's *t* test or Mann-Whitney *U* test. Categorical variables were reported as frequencies (percentages) and analysed using the Pearson's χ^2 or Fisher's exact test. A p value of less than 0·05 was considered statistically significant. All induced circulatory arrests were analysed as individual events. Alarms in the absence of induced or true circulatory arrest or severe haemodynamic instability (mean arterial pressure ≤45 mm Hg or pulse pressure ≤15 mm Hg) were regarded as false positive. Alarms were also regarded false positive in the case of an early termination of the alert by the re-detection of pulsatile photoplethysmography signal. The performance of the algorithm was evaluated for each iteration and reported by providing the sensitivity (the primary endpoint) to detect circulatory arrest with 95% CIs, the number of false positive circulatory arrest alarms, and the false positive alarm rate; the false positive alarm rate was calculated by dividing the number of false positive alarms by the number of hours of non-circulatory arrest data. All collected photoplethysmography data were analysed for false positive circulatory arrest alarms. Positive predictive values with 95% CIs were provided as well. The specificity was reported on the basis of 1-min intervals of pulsatile photoplethysmography signal correctly identified as non-circulatory arrest.[24] This approach was chosen in light of the differences in duration of non-circulatory arrest data per patient, and potential for multiple false positive alarms within a single patient. Sensitivity analysis was performed including only the first induced event of each individual patient to assess dependency in the data. In addition to the main analysis, post-hoc analyses were performed to calculate the sensitivity of the detection of spontaneous cardiac arrests as well as of the sensitivity of interruptions of blood flow through blood pressure cuff inflation. Statistical analyses were performed in SPSS (version 27.0).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

A total of 306 patients were enrolled in the study between March 14, 2022, and April 21, 2023. In total, 15 patients were excluded because of missing photoplethysmography or reference data related to technical issues or human error (appendix p 7). Therefore, 291 patients were included in the analysis, of whom 274 patients were in the TAVI group, seven patients were in the S-ICD group, and ten patients were in the ventricular tachycardia ablation group. In these patients, 324 circulatory arrests were induced in 214 patients and there were 278 h of non-circulatory arrest data. In 77 patients, no circulatory arrest was induced, consisting primarily of patients in the TAVI group without balloon dilatation.

The baseline characteristics are presented in table 1. The median age was 79 years (IQR 75–83); 80 years (75–84) in the TAVI group, 47 years (IQR 44–67) in the S-ICD group, and 62 years (IQR 55–74) in the ventricular tachycardia ablation group. In total, 167 patients (57%) were male and 124 (43%) were female; 219 (75%) had a white or fair Fitzpatrick scale skin type; and 204 (72%) had nil to sparse arm hair density. Patient characteristics did not differ between the consecutive iterations (appendix p 8).

The first training set consisted of 74 patients, with 70 induced circulatory arrests in 50 patients, and 44 h of non-circulatory arrest data. The sensitivity for circulatory arrest detection was 100% (95% CI 94–100%), with four false positive circulatory arrest alarms, resulting in a false positive alarm rate of 0·09 (table 2). The positive predictive value was 95% (95% CI 86–98%). The specificity for the detection of pulsatile photoplethysmography signal was 99·9% (99·7–100·0%) with analysis of 1-min intervals (table 3).

The second training set consisted of 66 patients, with 78 induced circulatory arrests in 50 patients, and 75 h of non-circulatory arrest data. The sensitivity for circulatory arrest detection was 100% (95% CI 94–100%), with six false positives, and a false positive alarm rate of 0·08 (table 2). The positive predictive value was 93% (95% CI 85–97%). The specificity for the detection of pulsatile photoplethysmography signal was 99·8% (99·6–99·9%; table 3).

The third training set consisted of 65 patients, with 79 induced circulatory arrests in 50 patients, and 68 h of

	All patients (n=291)	Transcatheter aortic valve implantation (n=274)	Subcutaneous implantable cardioverter defibrillator implantation (n=7)	Ventricular tachycardia ablation (n=10)
Age, years	79 (75–83)	80 (75–84)	47 (44–67)	62 (55–74)
Male sex	167 (57%)	156 (57%)	4 (57%)	7 (70%)
Female sex	124 (43%)	118 (43%)	3 (43%)	3 (30%)
BMI, kg/m²	27 (24–30)	27 (24–30)	27 (23–29)	24 (24–29)
Body surface area, m²	1·9 (0·22)	1·9 (0·22)	2·1 (0·21)	2·0 (0·16)
Medical history				
Hypertension	143 (49%)	139 (51%)	0	4 (40%)
Diabetes	83 (29%)	79 (29%)	0	4 (40%)
Smoking, current or former	155/265 (58%)	147/251 (59%)	3/6 (50%)	5/8 (63%)
History of cardiac arrest	7 (2%)	5 (2%)	2 (29%)	0
History of myocardial infarction	47/288 (16%)	40/271 (15%)	2 (29%)	5 (50%)
History of coronary artery disease	132 (45%)	125 (46%)	2 (29%)	5 (50%)
Moderate or severe aortic valve stenosis	271 (93%)	270 (99%)	0	1 (10%)
History of stroke or transient ischaemic attack	40 (14%)	39 (14%)	0	1 (10%)
History of atrial fibrillation	78/289 (27%)	78/272 (29%)	0	0
Left ventricular systolic function				
Good, ≥52%	187/288 (65%)	184/272 (68%)	3 (43%)	0
Mildly reduced, 41–51%	63/288 (22%)	58/272 (21%)	1 (14%)	4/9 (44%)
Moderately reduced, 30–40%	26/288 (9%)	22/272 (8%)	3 (43%)	1/9 (11%)
Severely reduced, <30%	12/288 (4%)	8/272 (3%)	0	4/9 (44%)
Medication				
β blocker	168 (58%)	155 (57%)	3 (43%)	0
Angiotensin-converting enzyme inhibitor	152 (52%)	14 (5%)	4 (57%)	2 (20%)
Calcium channel blocker	72 (25%)	70 (26%)	1 (14%)	1 (10%)
Mineralocorticoid receptor antagonist	41 (14%)	37 (14%)	3 (43%)	1 (10%)
Loop diuretic	112 (38%)	107 (39%)	2 (29%)	3 (30%)
Thiazide diuretic	38 (13%)	38 (14%)	0	0
Laboratory values of haemoglobin, mmol/L	7·9 (0·95)	7·9 (0·93)	8·4 (0·84)	9·1 (0·85)
Fitzpatrick scale				
I, white	24 (8%)	24 (9%)	0	0
II, fair	195 (67%)	185 (68%)	5 (71%)	5 (50%)
III, medium	57 (20%)	53 (19%)	2 (29%)	2 (20%)
IV, olive	13 (5%)	11 (4%)	0	2 (20%)
V, brown	1 (<1%)	1 (<1%)	0	0
VI, very dark brown	1 (<1%)	0	0	1 (10%)
Arm hair density				
Nil	96/286 (34%)	89/269 (33%)	3 (43%)	4 (40%)
Sparse	108/286 (38%)	104/269 (39%)	3 (43%)	1 (10%)
Moderate	71/286 (25%)	66/269 (25%)	1 (14%)	4 (40%)
Dense	11/286 (4%)	10/269 (4%)	0	1 (10%)
Wrist circumference, cm	17·0 (16·0–18·0)	17·0 (16·0–18·0)	15·6 (14·5–16·4)	17·2 (16·3–18·7)

Data are mean (SD), median (IQR), or n (%). Sex was self-reported. Smoking status was known for 265 (91%) patients, history of myocardial infarction for 288 (99%) patients, left ventricular systolic function for 288 (99%) patients, arm hair density scale in 286 (98%) patients, and history of atrial fibrillation in 289 (99%) patients.

Table 1: **Baseline characteristics for each group**

non-circulatory arrest data. The sensitivity for circulatory arrest detection was 100% (95% CI 94–100%), with two false positives, resulting in a false positive alarm rate of 0·03 (table 2). The positive predictive value was 98% (95% CI 91–100%). The specificity for the detection of pulsatile photoplethysmography signal was 100·0% (99·8–100·0%; table 3). Further details on the performances of the three training iterations are presented in tables 2 and 3 and figure 2.

The validation set consisted of 86 patients, with 97 induced circulatory arrests in 64 patients and 91 h of non-circulatory arrest data. The sensitivity for

	Training 1 (n=74)	Training 2 (n=66)	Training 3 (n=65)	Validation (n=86)
Intervention				
Transcatheter aortic valve implantation	72	63	62	77
Subcutaneous implantable cardioverter defibrillator implantation	1	1	2	3
Ventricular tachycardia ablation	1	2	1	6
Patients with induced events	50	50	50	64
Patients without induced events	24	16	15	22
Induced events				
Rapid ventricular pacing with balloon dilatation:* pre-dilatation	33	31	30	29
Rapid ventricular pacing with balloon dilatation:* valve placement	23	27	21	26
Rapid ventricular pacing with balloon dilatation:* post-dilatation	13	16	22	25
Ventricular fibrillation induction (defibrillation test)	1	1	2	4
Ventricular tachycardia induction	0	3	4	13
Total	70	78	79	97
Median duration of induced event, s	11 (9–16)	12 (10–16)	13 (9–15)	13 (10–16)
Hours of non-circulatory arrest data	44	75	68	91
True positive alarms	70	78	79	95
False negative alarms	0	0	0	2
False positive alarms	4	6	2	11
Unique number of patients with false positive alarms	3	5	2	11
False positive alarm rate	0·09	0·08	0·03	0·12
Sensitivity	100% (94–100%)	100% (94–100%)	100% (94–100%)	98% (92–100%)
Positive predictive value	95% (86–98%)	93% (85–97%)	98% (91–100%)	90% (82–94%)

Data are n, median (range), or value (95% CI). Primary and secondary endpoints did not differ in relation to patient or procedural characteristics, including sex and study site. The sensitivity is the primary outcome of this study. *Transcatheter aortic valve implantation.

Table 2: **Algorithm performance**

	Training 1 (n=74)	Training 2 (n=66)	Training 3 (n=65)	Validation (n=86)
Pulsatile photoplethysmography signal, classified as pulsatile: true negative, min	2660	4483	4078	5439
Non-pulsatile photoplethysmography signal, classified as non-pulsatile: true positive, min	15	20	17	25
False positive, min	2·0	8·0	1·0	3·5
False negative, min	0·0	0·0	0·0	0·5
Specificity for detection of pulsatile photoplethysmography signal	99·9% (99·7–100·0%)	99·8% (99·6–99·9%)	100·0% (99·8–100·0%)	99·9% (99·8–100·0%)

Data are n or value (95% CI). Specificity was calculated on the basis of 1-min intervals (instead of 1-h intervals) to improve interpretation given the short duration of false positive alarms.

Table 3: **Pulsatile and non-pulsatile photoplethysmography signal, expressed in minutes, for each training iteration and the validation set**

circulatory arrest detection was 98% (95% CI 92–100%). There were 11 false positive circulatory arrest alarms, and a false positive alarm rate of 0·12. The positive predictive value was 90% (95% CI 82–94%). The specificity for the detection of pulsatile photoplethysmography signal was 99·9% (99·8–100·0%). Further details are presented in tables 2 and 3 and figure 2. When only including all first circulatory arrest events (64 events), the sensitivity was 97% (95% CI 88–99%).

In the validation cohort, there were in total 75 interruptions to blood flow related to blood pressure cuff inflation in 11 patients (figure 3A). The sensitivity to detect these events was 97% (95% CI 90–100%) considering every measurement as a single event.

A total of nine patients had a spontaneous cardiac arrest, all during TAVI. Two patients had ventricular fibrillation, five had pulseless electrical activity (figure 3B), and two had asystole. All but one spontaneous cardiac arrest were detected by the circulatory arrest detection algorithm.

Discussion

The DETECT project is dedicated to developing a technological solution for automated cardiac arrest detection and alarming. In this DETECT-1 study, we

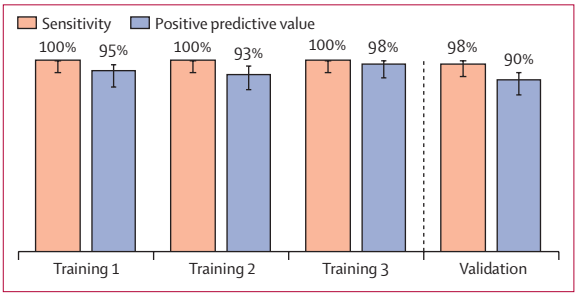

Figure 2: **Sensitivity and positive predictive value for circulatory arrest detection with 95% CI**

present the results of the development and validation of the circulatory arrest detection algorithm based on photoplethysmography using patient data of induced circulatory arrests. Relying solely on photoplethysmography data, induced circulatory arrest was able to be detected with high sensitivity and low false positives. These promising findings warrant the further development of this wearable technology to enable automated cardiac arrest detection and alarming in a home setting.

The early recognition of cardiac arrest is a crucial link in the chain of survival to enable the activation of an emergency medical response. Although more than 90% of patients with a witnessed cardiac arrest receive emergency medical treatment, this occurs for only 55% of all patients who have an unwitnessed cardiac arrest, and together with the longer treatment delays, this results in dismal survival chances of less than 5%.[9,14,25] The use of an innovative wearable biosensor technology could bridge the gap in OHCA recognition. The potential effect on OHCA survival of different biosensor sensitivities was recently estimated from OHCA data of the British Columbia Cardiac Arrest Registry.[14] Assuming that the biosensor for automated cardiac arrest detection was used in all previously unwitnessed cases, survival was expected to increase 2·3 times for sensor sensitivities of 90%, and 2·5 times for sensitivities of 100%.

Although an awaited technology, there are sparse data from small studies on the potential of automated circulatory arrest detection using smart devices. In a proof-of-concept study, a machine learning-based algorithm could distinguish cardiac arrest-associated agonal breathing from usual breathing sounds (including snoring and hypopnoea, etc).[26] ECG monitoring is well established to detect cardiac arrest, but continuous monitoring in a home setting is less feasible, sensitive to noise, and would not recognise pulseless electrical activity as a circulatory arrest.[13] For photoplethysmography, animal studies have shown the feasibility of the detection of induced haemodynamically unstable arrhythmias.[16,17]

Photoplethysmography is the main sensor technology of our cardiac arrest detection solution to be developed

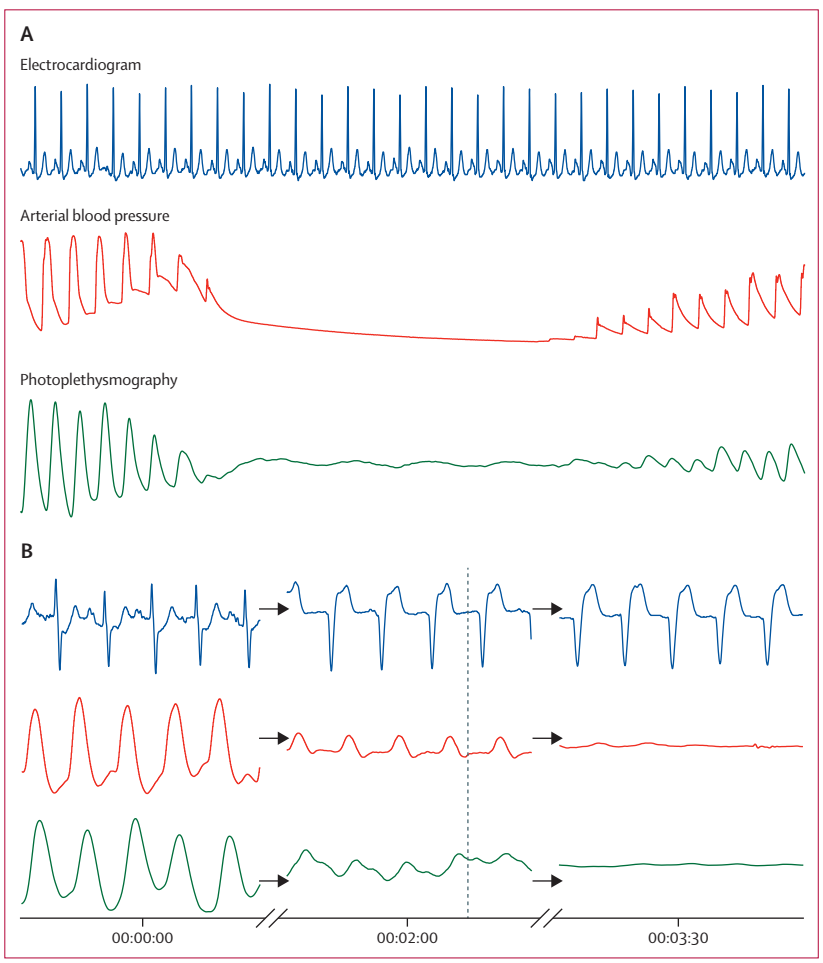

Figure 3: **Interruption of blood flow related to blood pressure cuff inflation in a patient in the TAVI group (A) and a patient with spontaneous cardiac arrest (B)**
The electrocardiogram signal is represented in blue, the invasively measured arterial blood pressure in red, and the photoplethysmography signal in green. (A) Blood pressure cuff inflation resulted in a short-lasting interruption of blood flow to the right arm (total duration 13 s), mimicking circulatory arrest. Before the event, the patient was in sinus rhythm with a blood pressure of 140/60 mm Hg. Inflation of the blood pressure cuff resulted in an interruption of blood flow to the right lower arm resulting in the flattening of the blood pressure and photoplethysmography curve. (B) An episode of spontaneous cardiac arrest based on pulseless electrical activity in a patient in the TAVI group related to acute aortic valve regurgitation after pre-dilatation. The initial recording (on the left) shows sinus rhythm with a blood pressure of 90/45 mm Hg and a normal pulsatile photoplethysmography signal. The panel in the middle is a recording of the initial haemodynamic instability with a ventricular rhythm on the electrocardiograph with a blood pressure of 55/35 mm Hg (mean arterial pressure 42 mm Hg) and decreased amplitude on the photoplethysmography recording. The dashed line in the figure indicates algorithm alarming for circulatory arrest. In the panel on the right, there is pulseless electrical activity, with a flat line on the arterial blood pressure and photoplethysmography curve. The episode was successfully detected by the circulatory arrest detection algorithm. After short-lasting cardiopulmonary resuscitation, the patient had a return of spontaneous circulation. TAVI=transcatheter aortic valve implantation.

and provides the direct assessment of blood flow, not specifically ventricular tachycardia or ventricular fibrillation, which are electrical processes. Therefore, whether cardiac arrest results from a shockable or non-shockable heart rhythm is irrelevant to the algorithm. Although photoplethysmography is also sensitive to noise, motion artifacts related to body movements mainly result in sharp peaks in the photoplethysmography signal not resembling a circulatory arrest episode where the

photoplethysmography signal flattens out. This is in contrast to the ECG signal, where motion artifacts can mimic ventricular tachycardia or ventricular fibrillation.[27] Although our study was performed under controlled circumstances, the collected data included challenging data fragments including atrial and ventricular arrhythmias, bradyarrhythmias, and operator-induced or patient-induced motion artifacts, or both. Moreover, the algorithm had to recognise a circulatory arrest within 5 s; this detection window was chosen because the circulatory arrest inductions were short-lasting. Despite these factors, the false positive alarm rate was low. Although the exact cause was not always clear, most false positive alarms seemed to be related to poor signal quality that resulted in a flattening of the photoplethysmography signal or true haemodynamic instability not fulfilling our strict criteria for circulatory arrest. It is expected that with longer detection intervals, false positive alarm rates will be even lower, similar to what was seen with the programming of longer detection intervals in ICDs.[28,29] This expectation is supported by the fact that the false positive registrations had a median duration of 20 s, after which the algorithm recognised spontaneous pulses and terminated the alarm appropriately. Additionally, after circulatory arrest induction, the algorithm detected the return of spontaneous circulation appropriately in all cases.

The implementation of automated alarming and deployment of rescuers will only be feasible with minimal false positives. Therefore, several other features can be incorporated to minimise false positive alarms. First, wearing detection will avoid false positive alarms when the wristband is detached or loose-fitting. Second, input from an accelerometer sensor to confirm or deny a circulatory arrest on the basis of analysis of user movements can improve accuracy. Third, an acoustic signal before the alarming of rescuers can enable the user to manually cancel the alarm. Fourth, the effect of motion artifacts can be mitigated by a dedicated algorithm, resulting in a more stable and reliable photoplethysmography pulse wave.

Motion artifacts could influence the sensitivity of the algorithm because a circulatory arrest might be missed in the case of inappropriate peak detection. However, this is not expected to be a major issue because an eventual physical collapse after cardiac arrests will generally be followed by the absence of any body movements. The single false negative alarm of a spontaneous cardiac arrest in our study was related to a noisy photoplethysmography signal resulting from the immediate resuscitative interventions of the medical team. The two induced circulatory arrest events that were missed occurred during episodes of poor signal quality, underlining the importance of a photoplethysmography sensor resistant to noise. In this light, it is important to emphasise that in contrast to atrial fibrillation detection algorithms, a real-time circulatory arrest detection algorithm should be able to handle the photoplethysmography signal, despite noise that might lead to poor signal quality.[30] The handling of noise is further explained in the appendix (pp 4–5).

The detection of circulatory arrest did not differ according to arrest induction method, but all false positive alarms in the validation set were in patients in the TAVI group. No predictors of false positive alarms could be identified. Additionally, sensitivity did not differ in relation to patient or procedural characteristics. Blood flow interruptions induced by cuff inflation were detected correctly as well. Moreover, robustness of the algorithm was confirmed by the appropriate detection of spontaneous circulatory arrests in all but one case, albeit in a small sample of patients.

Further study is needed to provide an external validation of algorithm performance as well as to establish its performance in a larger sample of spontaneous cardiac arrests (sensitivity) and during normal daily activities (false positives). When a reliable performance is reached in a real-world setting, a connection with the Dutch Citizen Rescuer Network (HartslagNu) is planned to be established. Additionally, a systematic evaluation of populations who might benefit from this technology, including cost-effectiveness, needs to be performed. Intended populations could include patients at an increased risk of sudden cardiac death, for example those with a family history of sudden cardiac death, cardiomyopathies, or post-myocardial infarction.

Despite its promising findings, it is important to acknowledge the study's limitations. Arterial line insertion was not always in the same side as where the wristband was applied (ie, it could be inserted in the contralateral arm or femoral artery); therefore, a true compromise of radial arterial blood flow might have been missed and could have resulted in an overestimation of false positive alarms. All methods of circulatory arrest induction resulted in acute haemodynamic compromise; the algorithm performance needs to be established for more gradual forms of cardiac arrest, as is more often the case with non-shockable rhythms. False positive alarms were only assessed by analysing the photoplethysmography signal recorded during the cardiac procedure; the number of false positive alarms during daily life use, where more motion artifacts can be expected, still needs to be investigated. Future studies investigating this aspect will also provide insight into whether and where additional sensor information needs to be incorporated into the algorithm to prevent potential false positive alarms. Additionally, the algorithm performance needs to be studied in the setting of spontaneous cardiac arrests. The DETECT-1 study results justify taking these next steps and warrant the further development of this potential breakthrough technology.

In conclusion, the automated detection of circulatory arrest using a photoplethysmography wristband is feasible with excellent sensitivity and low false positives.

Further study is needed to assess algorithm performance in spontaneous cardiac arrests, and to minimise false positive alarms using additional sensor input. If available for automated cardiac arrest detection and alarming in a home setting, this breakthrough technology could improve survival chances from unwitnessed OHCA.

Contributors

NTBS, MAB, RJB, ER, EB, PCS, NvR, and JLB conceptualised the study. RE, NTBS, MM-R, KV, S-CY, NvM, and JLB curated the data. RE, NTBS, EB, NvR, and JLB did the formal analysis. NTBS, ER, EB, PCS, NvR, and JLB acquired funding. RE, NTBS, MM-R, KV, S-CY, NvM, EB, NvR, and JLB contributed to the investigation. RE, KE, NTBS, EB, NvR, and JLB contributed to the methods. RE, NvR, and JLB contributed to the project administration. PCS, NvR, and JLB provided the resources. KE and PCS ran the data on the software. MAB, RJB, ER, NvM, EB, PCS, NvR, and JLB supervised the study. RE, NTBS, KE, PCS, NvR, and JLB validated the data. RE, KE, and JLB contributed to visualisation. RE, NvR, and JLB wrote the original draft. NTBS, KE, MAB, RJB, MM-R, KV, S-CY, ER, NvM, EB, PCS, and NvR reviewed and edited the manuscript. RE, NTBS, KE, MAB, RJB, MM-R, KV, S-CY, ER, NvM, EB, PCS, NvR, and JLB gave final approval of the manuscript before publication.

Declaration of interests

KE is a data scientist at Corsano Health. RJB received a research grant from Biosense Webster, and payment for a lecture from The Cardiovascular Education Institute. KV received a research grant from Medtronic; consulting fees from Medtronic, Abbott, and Biosense Webster; a speakers fee from Philips; participates in the advisory board of Medtronic; and received educational grants from Medtronic, Abbott, and Biosense Webster. S-CY is a consultant of Boston Scientific; has received research grants from Biotronik, Medtronic, and Boston Scientific; received personal payments for presentations from Boston Scientific, Biotronik, and Medtronic; and his institution received payment for his participation on a Data Safety Monitoring Board from Boston Scientific. ER received consulting fees from Corsano Health. NvM received grants from Abbott Vascular, Boston Scientific, Medtronic, Edwards Lifesciences, Daiichi Sankyo, and AstraZeneca; received personal consulting fees from Abbott Vascular, Boston Scientific, Medtronic, Anteris, JenaValve, Daiichi Sankyo, AstraZeneca, Amgen, Siemens, and Pie Medical; and received payment for presentations from Abbott Vascular, Biotronik, Amgen, Daiichi Sankyo, Medtronic, and Boston Scientifc. PCS is the CEO of Corsano Health. NvR received a research grant from the Dutch Heart Foundation related to this manuscript; received research grants from Biotronik, Abbott, Medtronic, and Philips, not related to this manuscript; and speaker fees were received from Abbott, Bayer, RainMed, and Microport, not related to this manuscript. All other authors declare no competing interests.

Data sharing

The most recent version of the study protocol has been included on our website, www.detect-study.com/partners/participating-centers/. Previous versions can be accessed upon request to the corresponding author. Individual participant data that underlie the results reported in this Article will be made available, after de-identification (text, tables, figures, and appendices). This includes the final versions of data used for analysis and data dictionaries needed to understand the data. The data repository DANS data stations will be used to guarantee the long-term accessibility of the research data from this project. Data will be available immediately following publication, with no end date. The data will be shared with investigators whose proposed use of the data has been approved by the review committee identified for this purpose. To gain access, data requestors will need to sign a data access agreement. Investigators wishing to access these data should contact the corresponding author (judith.bonnes@radboudumc.nl).

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