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REVIEW

The AngelMed Guardian® System in the Detection of Coronary Artery Occlusion: Current Perspectives

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Abstract: Total ischemic time, which specifies the time from the onset of chest pain to initiation of reperfusion during percutaneous coronary intervention, consists of two intervals: symptom to door time and door to balloon time. A door to balloon time of 90 mins or less has become a quality-of-care metric in the management of ST elevation myocardial infarction (STEMI). While national efforts made by the American College of Cardiology (ACC) and American Heart Association (AHA) have curtailed in-hospital door to balloon time over the years, a reduction in pre-hospital symptoms to door time presents a challenge in modern interventional Cardiology. Early and complete revascularization has been associated with improved clinical outcomes in MI and strategies that may help reduce symptom to door time, and thus the total ischemic time, are crucial. Rapidly evolving ST-segment changes commonly develop prior to ischemia-related symptom onset, and are detectable even in patients with clinically unrecognized silent MIs. Therefore, a highly intelligent ischemia detection system that alerts patients of ST segment deviation may allow for rapid identification of acute coronary occlusion. The AngelMed Guardian® System is a cardiac activity monitoring and alerting system designed for rapid identification of intracardiac ST-segment changes among patients at a high risk for recurrent ACS events. This article reviews the clinical studies evaluating the design, safety and efficacy of the AngelMed Guardian System and discusses the clinical implications of the device.

Keywords: acute coronary syndrome, myocardial infarction, ST elevation myocardial infarction, ischemia monitoring, electrocardiography

Introduction

Atherosclerotic cardiovascular disease (ASCVD) represents a common yet preventable condition and affects 18.2 millions of individuals aged ≥20 years in the United States.[1] Approximately 70% of these people have never had a previous episode of myocardial infarction (MI), whereas about 30% are those who suffer from a recurrent MI. In addition, silent MI (i.e., MI that escapes clinical recognition) is more common than previously thought and accounts for ≥20% of MI cases.[2,3] Such high numbers place MI among one of the leading causes of death in Western countries.

Over the past two decades, advances in coronary reperfusion strategy using angioplasty or thrombolytic therapy have dramatically transformed the management of acute MI. However, the rate of rapid reperfusion may affect both the short-term and long-term prognosis of patients with ST-elevation myocardial infarction (STEMI).[4–6] Therefore, given the prognostic implications of the total ischemic

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time (i.e., a composite of symptom to door [S2D] and door to balloon [D2B] time), a delay of diagnosis tends to prevent the optimal derivation of benefit from these treatment modalities.

Studies have shown that the total ischemic time is an independent predictor for infarct size among patients with STEMI.[7,8] The duration of myocardial ischemia secondary to coronary occlusion has a direct relation to irreversible cardiomyocyte injury.[9] Specifically, an ischemic time of greater than 20 mins has been associated with cardiomyocyte death.[10] Further, the majority of irreversible damage to the myocardium and lethal arrhythmia develop within the initial 60 mins following a coronary occlusion.[4,5,11–16] These findings indicate the pivotal role of early detection and intervention in minimizing myocardial necrosis and preventing associated complications.

A key quality metric in the management of STEMI is to reduce ischemic time by reestablishing blood flow to jeopardized myocardium as early as possible. Based on the current practice guidelines, an occluded artery should be reperfused with fibrinolytic agent in 0.5 hr or revascularized with percutaneous coronary intervention (PCI) in 1.5 hr from patient's arrival in the emergency department. Prior studies have shown that only 20% of patients arrive at the hospital in 60 mins after the onset of symptoms, which represents the timeframe that reperfusion therapy may derive the greatest benefit.[17–19] Despite shortened door to needle and D2B time that have been translated into decreased mortality in STEMI,[20–24] the S2D time remains at 2.7 hrs on average and can be much longer due to a number of sociodemographic, cognitive, behavioral, technological and illness factors.[25] It has been shown that the relative risk of death at 1 year is increased by 7.5% with each 30 mins delay in reperfusion therapy. Consequently, early hospital arrival may be beneficial.[26]

Current Barriers to Reducing Symptom-to-Door Time

The current methodology employed for the diagnosis of ACS events relies on symptoms, electrocardiogram, and sensitive biochemical markers, with patients relying on symptoms alone for prompt presentation to a medical facility. Lack of improvement in symptom-to-door time may be attributed to patient misconceptions of heart attack symptoms,[5] patient denial or anxiety, clinically unrecognized or misdiagnosed MI, and failure to detect electrocardiography (EKG) findings indicative of MI.[27,28] It should be noted that unrecognized or misdiagnosed MI and failure to detect EKG findings indicative of MI would have to be in the outpatient setting to affect symptom-to-door time.

Of note, patient education to improve symptom recognition as well as to prevent delayed presentation to medical care did not significantly improve outcomes in acute myocardial infarction (AMI).[29] Furthermore, a substantial proportion of individuals with MI do not have typical chest discomfort and therefore may not seek medical attention promptly.[27,28,30] Silent MI is defined as myocardial ischemia (evidenced by ischemic ST-segment changes, reversible regional wall motion abnormality, or reversible myocardial perfusion defect) in the absence of chest pain or other symptoms associated with ischemia (termed "anginal equivalents").[31] It has also been shown that around 2–4% of the population has myocardial ischemia that is clinically silent but detectable with ambulatory monitoring or exercise treadmill.[32] Silent MI is commonly noted in subjects who have ASCVD risk factors such as hypertension (prevalence 1.3–2.4% for men and 1.5–3.3% for women),[33,34] a prior history of CVD, female gender, diabetes (prevalence 4–37%), and the elderly (prevalence 0.3–5.4%).[28,35–39] These patients represent a major proportion of undertreated high-risk ACS population and have substantially greater all-cause death and cardiovascular death compared to symptomatic MI patients.[40] Additionally, patients with chronic angina may not react to the onset of MI when they find it difficult to discern any change in symptoms from MI onset compared to their ongoing background level of chest discomfort and pain.

Another impediment to the implementation of timely treatment is mis- or under-diagnosis of acute thrombotic occlusion. Traditional 12-lead surface EKG has demonstrated limited sensitivity and specificity for detecting posterior or lateral MI. Thus, posterior MI causing isolated ST depression in anterior leads is often misinterpreted as anterior wall ischemia.[41] The diagnosis of posterior wall MI is challenging due to inconsistent presentation on EKG and the relatively minor contribution to QRS complex in the anterior leads from the posterior myocardium.[42] Therefore, physicians recognized a very small fraction of posterior infractions with an anterior segment depression due to a prolonged delay from the performance of EKG to PCI. Furthermore, a reduction in life expectancy and quality, higher hospitalization rates, and increased risk of sudden death were a result of the morbidity associated with delays in seeking treatment.[43]

The AngelMed Guardian® System: Device Design and Components

State-of-the-Art Alarm Design

The application of multimodal alarm systems, including vibrotactile, auditory, and visual alarm systems can be seen in daily practice within the healthcare system.[44–50] The effectiveness and reliability of these clinical alarm systems are influenced by various human factors, such as sensory perception, cognitive capacity and behavioral processes.[51,52] For example, the optimal use of auditory or visual alarms in patients can be limited by auditory or visual impairment.[53] Similarly, alerting via vibration alone also presents problems in patients with decreased vibration sensitivity.[45] It has been shown that vibrotactile alarms, in combination with visual and auditory alarms, are far more superior in alerting compared to monomodal alerting systems (vibrotactile, visual or auditory alarms alone).[46] Thus, an intelligent clinical alarm system is one that is designed in a patient-centered manner, takes physiological variance into account and reflects trigger severity for adequate triage.[54–56]

The utilization of audio-visual alarms in patients suffering from cardiovascular diseases, such as those used in bedside monitors and implantable cardioverter-defibrillators, is widespread.[57–60] Given the clinical significance of urgency associated with treatment of myocardial ischemia, and the unchanged symptom-to-door time over the years, the AngelMed Guardian System has been designed as a patient-focused, multimodal, highly sensitive alarm system that detects EKG changes in real-time for prompt presentation to a medical facility.[47] Further, a more definitive pre-hospital diagnosis of an ischemic event through the Guardian System may result in the reduction of D2B times through effective triage decisions when the patient presents at the hospital door.[61]

Components of AngelMed Guardian System

The AngelMed Guardian System consists of an implantable medical device (IMD) and an external device (EXD). The size of the IMD is similar to that of a single-chamber pacemaker. The miniature IMD is subcutaneously placed in the upper-left region of the anterior chest, and senses myocardial electrical changes from a standard steroid-eluting lead that attaches to the right ventricular apex.[62,63] The Guardian programmer is configured to communicate with the IMD and retrieve EKG data for analysis. The IMD continuously checks for ST-segment deviation and other electrocardiographic alterations, such as irregular heartbeats or rhythms. In case of an event, the IMD notifies the patient by sending vibrating alarms, whereas the EXD beeps and flashes red or yellow indicators.[48] The device design and components of the AngelMed Guardian System can be seen in Figures 1 and 2.

Alarm Types That Reflect Event Mapping

The ST-segment denotes the horizontal, isoelectric section of the electrocardiogram between the S wave and the T wave that represents the interval between depolarization and repolarization of the ventricle. Every 90 s, the Guardian analyzes a 10-s intracardiac electrogram. The 24 hr average ST-segment level, average PQ segment level, R-wave height, and the RR interval (i.e. instantaneous heart rate) are calculated for each electrocardiogram sample. For every heartbeat waveform in the electrocardiogram sample, the ST segment deviation relative to the preceding PQ segment level is calculated and this difference is compared to corresponding difference in the patient's 24 hr composite baseline to derive a "ST shift". The percentage of ST shift ("ST-Shift%") is normalized in reference to the amplitude of the R wave, and is then compared against the patient's ST-shift detection threshold (i.e., 3 standard deviations from the patient's baseline range, as determined by the Guardian programmer's Autopick function and as calculated upon a prior 10–14-day sample of data). The Guardian System captures both positive and negative ischemia detection thresholds as ST-shift%. The intracardiac electrogram (ICEG) denoting the ST-shift% is obtained in a patient-specific manner based on comparison with a 24 hr baseline ST-shift at various heart rate ranges. To characterize whether a particular ST-segment shift is indicative of acute ischemia, the IMD utilizes these heart rate-dependent thresholds, with ST-segment depressions registered at higher heart rates. The IMD allows the detection thresholds for a positive ST shift% to be set at different levels than the thresholds for a negative ST shift%. This not only allows for lower false-positives but also differentiates ST-segment elevations from depressions. If abnormal rhythm or ST Shift % is noted, the interval between the sampling of electrograms shorten to once every 30 s. Events recorded by the Guardian System are mapped to different alarm types outlined in Table 1.

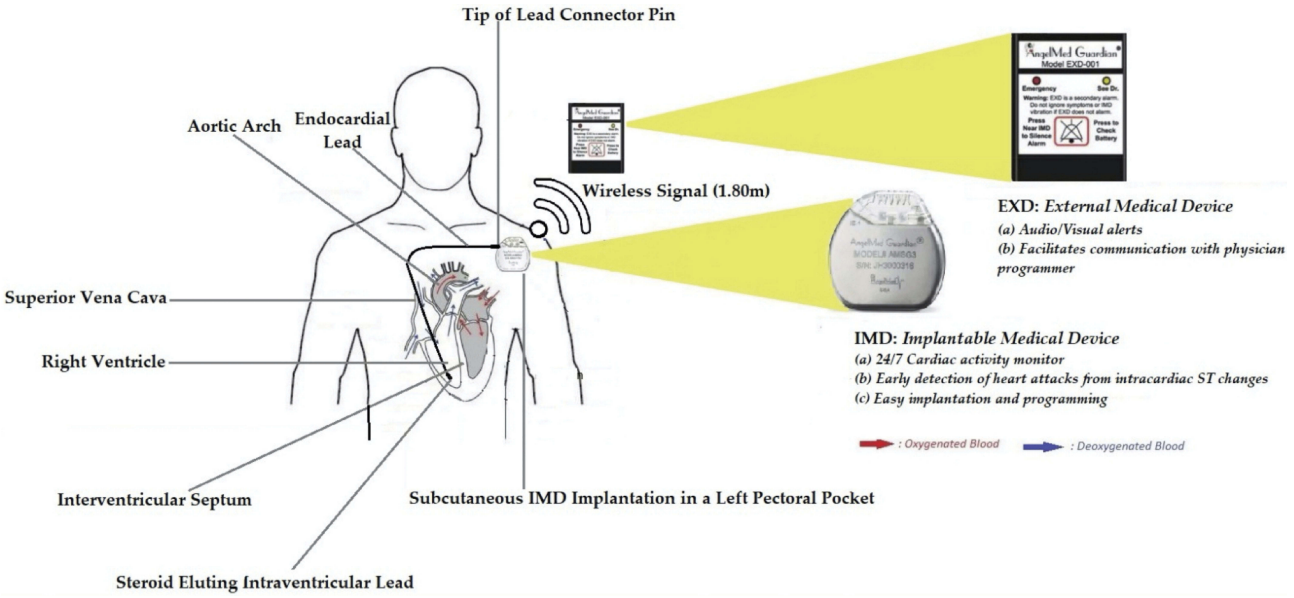

Figure 1 AngelMed Guardian® system device design and components.

Figure 2 Implantable medical device (IMD) and external medical device (EXD).

Proof-of-Concept Study, CARDIOSAVER, DETECT and ALERTS Trials

Alterations in the ST-segments and T waves are the earliest electrocardiographic findings of myocardial ischemia. In STEMI patients, acute coronary artery occlusion is indicated by rapid and progressive alterations in the ST-segments.[64] Human studies have shown that ST-segment deviation may develop within 15 s after obstructing a coronary vessel.[15] This finding justifies the importance of real-time monitoring of ST-segment for detecting myocardial ischemia without relying solely on non-specific symptoms. Various clinical studies have attempted to devise patient alerting systems via continuous surface-based EKG monitoring for this purpose. The timeline for the clinical studies of the AngelMed Guardian System is outlined in Figure 3. These evidence generating studies for the AngelMed Guardian System are summarized in Table 2.

Proof-of-Concept Study

During the early 2000's, several human studies began to assess the ability of a temporary pacemaker lead to measure right ventricular (RV) apical voltage during coronary artery occlusion among individuals undergoing percutaneous transluminal coronary angioplasty. The investigators concluded that ST-segment changes arising as a result of coronary occlusion were magnified when recorded from an intracardiac RV apical electrogram as compared to when recorded from the skin surface.[15]

CARDIOSAVER (2005) and DETECT (2006) Studies

CARDIOSAVER was a Phase I clinical feasibility study conducted in Brazil. The primary objective of the CARDIOSAVER study was to test the performance of the Guardian system in detecting intracardiac ST shifts resulting from subendocardial and transmural ischemia. The study enrolled 20 subjects with an increased risk of a recurrent coronary occlusion and at least one of the following: (1) ischemia on an exercise stress test; (2) stenosis of a coronary artery on angiogram; or (3) clinical indication for stenting and/or angioplasty. Following the implantation

Table 1 AngelMed Guardian® System Alarm Types

Alert Type	Qualifying Event Category	IMD Function	EXD Function	Data Storage
High Priority Alarms				
Emergency alerts (Patient calls 911 for prompt arrival at a medical facility	3 successive 10-second electrogram segments with each segment at least six out of eight beats with ST shifts that exceed the detection threshold while the heart rate is within normal range	Vibrates	Beeps in a synchronized 3-2-3-2 pattern, and flashes a red light	24 hrs before alarm through 8 hrs after alarm
Low Priority Alarms				
See Doctor alerts	(a) Abnormal heart rates (Tachycardia and bradycardia) (b) Persistent irregular rhythms (c) Loss of signal (Lead detachment/low battery/general malfunction)	Vibrates	Beeps once after each 7 second interval, and flashes a yellow light	24 hrs before alarm and at time of alarm
None	Save data in the See Doctor manner but do not alert the patient	N/A	N/A	24 hrs before alarm and at time of alarm
Ignore	Neither save the data nor alert the patient	N/A	N/A	N/A

of the device, subjects underwent a 3 mins long balloon occlusion of the target artery and intracardiac ST-segment changes were found to be significant in the case of vessel stenosis with no collateral flow. This finding provided evidence that the AngelMed Guardian System may potentially allow for early detection of myocardial ischemia and initiation of life-saving interventions.[47,49]

DETECT was another phase I study aimed to assess the safety profile of the Guardian system. The study also explored ST-segment shift thresholds for detecting myocardial ischemia. Overall, the CARDIOSAVER and DETECT studies enrolled 37 patients at risk of recurrent thrombosis who received Guardian System implantation. The median follow-up duration was 1.52 years. The results indicated that the Guardian System is a safe and feasible device for detecting ischemia and notifying patients. It is concluded that intracardiac ST shifts lasting more than 2 mins and exceeding three standard deviations from normal daily may be a threshold with acceptable sensitivity and specificity for identifying coronary thrombosis and occlusion secondary to ruptured atherosclerotic plaques. In contrast to the median delay of 2–3 hrs after the onset of symptoms, the time from alert by the Guardian System to hospital arrival was 19.5 mins.[47,49]

ALERTS Trial

The ALERTS trial (NCT: 00781118) was a Phase III prospective, randomized, multicenter trial that enrolled 1020 subjects at high-risk of MI due to acute coronary syndrome or bypass surgery. A total of 907 subjects received implantation of the Guardian System, and were randomized in a 1:1 ratio into Treatment (Alarms activated) and Control (Alarms deactivated-for first 6 months) groups. After the six-month randomization period, alarms were activated in the control arm and all subjects were followed until study termination (mean duration of 3.05 years). The primary safety endpoint of the ALERTS trial was to determine if the fraction of subjects free from system or device-related complications was greater than 90%. A total of 30 subjects developed 31 complications, resulting in a 96.7% complication-free rate, meeting the primary safety endpoint. A total of 20 participants had the device removed with eleven of those participants experiencing infection. Device-related complications of the AngelMed Guardian System in the ALERTS trial are outlined in Table 3.

The primary efficacy endpoint was the composite of cardiac or unexplained death, new Q-wave MI, and time-to-door for a confirmed occlusive event at a medical facility >2 hrs. "Look-back" intervals among the control arm were used to determine subject arrival for an event that exceeded the 2 hr window. The AngelMed Guardian System did not significantly reduce the occurrence of the primary composite endpoint using a 7-day look-back window with 16 (3.8%) events occurring in the treatment group (pt) versus 21 (4.9%) events occurring in the control group (pc) (Posterior probability [Pr] = 0.786).

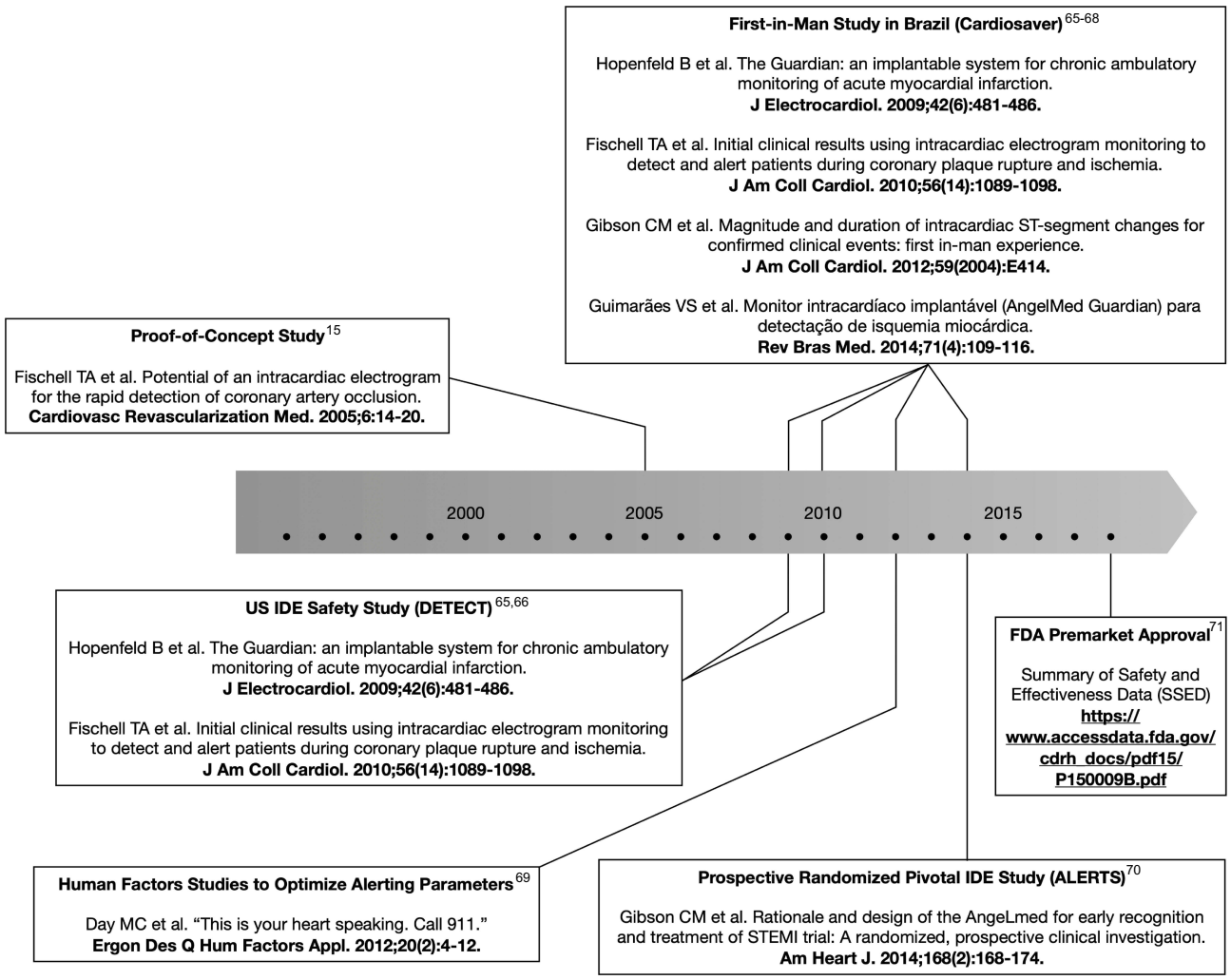

Figure 3 Timeline for the clinical studies of the AngelMed Guardian® system.

A trend towards significant difference was seen using a 90-day look-back window (3.8% vs. 6.8%; Pr [pt < pc] = 0.974), which was the furthest look-back window used, since it was the longest period between scheduled check-up visits where new Q-waves could be detected. Using a pre-specified 7-day look back window, the alarms significantly reduced detection to arrival time at a medical facility (51 mins versus 30.6 hrs; Pr [pt < pc] >0.999). When a 90-day look back window was used, the control group median time-to-door arrival further increased to 22 days. In addition to this, use of a "dual baseline" (pre-implant EKG and EKG at randomization) for the Q-wave analysis demonstrated statistical significance for the reduction in primary composite endpoint.

Secondary endpoints comprises the individual components of the primary composite endpoint as well as the median time to ED arrival. Authors did not complete statistical analyses for cardiovascular death as only 4 occurred in the trial. Similar to the primary endpoint, new Q-wave MI was lower in the treatment group (10 [2.4%] vs. 14 [3.3%], which increased to 7 [1.7%] vs. 13 [3.0%] in an additional dual-baseline analysis), but this difference was not statistically significant. A statistically significant reduction in number of subjects with late arrival when using the 90-day look-back window was seen, with 4 (0.9%) in the treatment arm and 17 (3.8%) in the control arm. Additionally, while the endpoint was defined for late arrivals, rather than those <2 hrs, it should be noted that the arrival pattern for all confirmed events that occurred for the control and treatment groups were different with arrival ≤2 hrs for 85% of the events in the treatment arm compared to only 5% of the events in the control arm.

An expanded analysis that included all emergency department (ED) visits during the randomized period of the trial, and also those which occurred after the randomized portion of the trial, when all subjects had their alarms turned on, was

Table 2 Evidence Generating Studies for the AngelMed Guardian® System

Study	Authors	Study Population	Study Design	Primary Endpoint	Secondary Endpoint	Results
Proof of Concept Study[15]	Fischell T. A. et al	n = 17 vessels, 14 patients that underwent balloon occlusion of an epicardial artery	Case series	Feasibility of intracardiac electrogram recording for the detection of ST-segment shift during balloon occlusion in the setting of PTCA	N/A	Mean ST-segment shift of 36.4%, relative to the QRS amplitude with intracardiac lead, within 2 min of balloon occlusion vs. 10.1% for surface lead; p = 0.00011
Magnitude and Duration of Intracardiac ST-Segment Changes for Confirmed Clinical Events: First in-man Experience[71]	Gibson C. M. et al	n = 76 high risk patients with coronary artery disease	Case series	Size and duration of the intracardiac ST-segment changes for true positive emergency alarms (EAs) corresponding to clinically relevant recurrent ischemic events confirmed by conventional tests (EKG, cardiac enzymes and angiographic vessel occlusion)	N/A	For a total of 21 EAs detected by intracardiac RV lead, size and duration of the ST-shift% changes did not correspond to the severity of the events as measured using conventional tests. (a) For positive EAs, mean ST-shift% was −22.4% with a mean duration of 56 mins (b) For negative EAs, mean ST-shift% was 22.6% with a mean duration of 78 mins (c) Mean ischemia detection threshold were −15.9% and 17.5%; p<0.01, indicating asymmetrical distribution of normal daily ST-shift%
First-in-Man Study of the Guardian System (Cardiosaver)[72]	Hopenfeld B et al	n = 20 patients with (1) ischemia on an exercise stress test; (2) stenosis of a coronary artery on angiogram; or (3) clinical indication for stenting and/or angioplasty	Phase I clinical feasibility study (Brazil)	Performance testing of Guardian system in detecting intracardiac ST shifts resulting from subendocardial and transmural ischemia	N/A	Successful demonstration of proof-of-concept with improvements in device design and ischemia detection algorithm

(*Continued*)

Table 2 (Continued).

Study	Authors	Study Population	Study Design	Primary Endpoint	Secondary Endpoint	Results
US Investigational Device Exemption Safety Study of the Guardian System (DETECT)[72]	Hopenfeld B et al	n = 17 patients who were survivors of a prior ACS event or bypass with additional risk factors	Phase I clinical feasibility study (USA)	(1) Reliability of the Guardian system's "Autopick function" to identify ischemia detection thresholds tailored to individual's 24 hr ST segment variability (rest and exercise) (2) Safety of Guardian system	N/A	(a) At rest, average ST segment shift across all patients was within 5% (ST segment shift % = (Current ST deviation – ST deviation of 24 hr baseline/R-wave height of a 24 hr baseline) x 100 (b) Post-exercise stress test, average ST shift% was −40% (c) ST shift % variation showed that 90% of fluctuations were < 6% indicating noise-free, stable function
ALERTS Trial[65]	Gibson C. M. et al	n = 907 patients at high-risk of MI due to acute coronary syndrome or bypass surgery	Bayesian adaptive, phase III prospective, randomized, multicenter trial	Efficacy: Composite of cardiac or unexplained death, new Q-wave MI, and time-to-door for a confirmed occlusive event at a medical facility >2 hrs Safety: Fraction of subjects free from system or device related complications >90%	(1) Individual components of primary end point (2) Superior false positive rate (FPR) for Guardian alerting (3) Ability to detect silent MIs (4) Timely presentation to a medical facility due to Guardian alerting in STEMI, NSTEMI and ACS patients (5) Ability to detect other clinically relevant conditions for timely presentation to a medical facility	(a) Primary efficacy endpoint not met (met with use of a dual-baseline for EKG) (b) Guardian system significantly reduced detection to arrival time at a medical facility (51 mins in alarms activated versus 30.6 hrs in alarms deactivated; Pr >0.999) (c) Met primary safety endpoint with 96.7%complication-free rate, Pr >0.9999 (d) FPR in alarms activated was 0.164 vs 0.678 in alarms deactivated; p<0.001 for non-inferiority (e) In treatment group (alarms activated), median symptom-to-door times for ACS, all MIs and STEMI were 1.04 h, 1.0 h and 0.75 h, respectively (f) Guardian system detected 108 other clinically relevant events (atrial fibrillation, anemia, bradycardia, bundle branch block, hypokalemia, tachycardia, transient heart block)

Table 3 Device-Related Complications of the AngelMed Guardian® System in the ALERTS Trial

Complication	Number of Events/Total Subjects	Percentage (%)
Cardiac perforation	2/907	0.22
Erosion	3/907	0.33
Infection	11/907	1.21
Lead misplacement	4/907	0.44
Device defect	2/907	0.22
Lead malfunction	1/907	0.11
Signal loss secondary to dislodgement or malfunction of the lead	2/907	0.22
Pain at or near implantation site	5/907	0.55
Visible bump at site of implantation	1/907	0.11
Total	30/907	3.3 (96.7% complication-free rate)

also completed. The results of the expanded analyses revealed an 18.2% positive predictive value (PPV) for the ALARMS OFF (symptoms only) group versus a positive predictive value (PPV) of 25.8% for the ALARMS ON (alarm with or without symptoms) group, though this difference was not statistically significant. Interestingly, the ALARMS ON group had a false-positive rate of 0.164 per person-year which was statistically lower than the ALARMS OFF group, which had a false-positive rate of 0.678 per person-year. Further, the Guardian System detected 42 acute coronary events in asymptomatic subjects.

Another important aspect of care was the evaluation of the subject's own perception of the disease in relation to mental and physical health status. To throw light on this, the ALERTS Quality of Life (AQOL) study, with the use of two established quality of life (QOL) instruments (EuroQOL EQ-5D and MacNew) and a custom-designed QOL survey, was designed to assess certain aspects of ALERTS subjects lives, such as anxiety and productivity. All the surveys demonstrated a significant improvement in subjects' quality of life. After Guardian alerting was enabled, 70% of the subjects reported an improvement in the quality of life at 6 months. This included success in resuming work, normal day-to-day recreational activities and improvement in health issues.

Data collected via the ALERTS trial have provided evidence that the Guardian System has a superior accuracy in alerting for coronary occlusion and subsequent ischemia when compared to patient-perceived symptoms alone. An expanded statistical analysis performed on follow-up data of the post-randomization period demonstrated a reduction in false-positive rate (patient presentations without an occlusive event) when compared to patient-perceived symptoms alone. Moreover, it was also shown that the AngelMed Guardian System was able to identify asymptomatic coronary occlusion (silent MIs) and prompt the patient to seek medical attention.[65]

Future Perspectives

The AngelMed Guardian System has regulatory approval in Europe and Brazil and received approval by Food and Drug Administration for use in the United States. A post-approval study design has been accepted by the FDA which will investigate the diagnostic accuracy of the AngelMed Guardian System in a commercial environment, and to assess the patient and physician training programs. A minimum of 500 patients with a history of ACS who remain at high risk for recurrent occlusive events are to be included in a prospective, non-randomized, single-arm, event-based, multi-center trial, for the purpose of accruing 314 ACS events adjudicated as true positive or false positive. The co-primary endpoint will assess the non-inferiority of positive predictive value (PPV) and false-positive rate (FPR) of the AngelMed Guardian System relative to what was found in the ALERTS trial. Secondary endpoints consist of the frequency of occlusive coronary events detected only by the Guardian System (i.e., silent ACS events or silent MIs) and symptom-to-door times.

There remains an unmet clinical need to develop strategies that allow for swift and accurate detection of thrombotic coronary occlusion for optimal secondary prevention in a high-risk population. Ischemia-detecting algorithms have been incorporated and tested in newer generations of implantable cardioverter-defibrillators (ICDs) that are originally designed to prevent sudden cardiac death from ventricular arrhythmia. For instance, the prospective ESTIMATION trial demonstrated that the use of ICD with a continuous ST-monitoring via intracardiac EKG was safe and effective for detecting asymptomatic myocardial ischemia, with a sensitivity, specificity, and negative predictive value of 75.0%, 72.5%, and 93.5% among participants who underwent myocardial perfusion imaging.[66] The Guardian System is the first implanted device in ambulatory subjects with advanced multivessel cardiac disease to provide ST-segment shift alerting,

thereby helping in the detection of a disease process with high morbidity and mortality, where earlier intervention can result in clinical benefit. The Guardian System alert has the capability to accurately recognize coronary occlusion as compared to patient-perceived symptoms alone. Results from randomized clinical trials have shown that even in the absence of symptoms, the Guardian System can precisely detect asymptomatic ACS events (silent MIs), thereby prompting the patients to seek medical attention. The ALERTS clinical trial has provided evidence for both safety and efficacy of this novel myocardial ischemia detection system. Moreover, there is an extensive list of benefits to patients receiving implantation of the Guardian System. While smartwatches and smartphone algorithms are showing great promise to identify cardiac arrhythmias, the reliable detection of coronary ischemia necessitates a highly intelligent alarm system superior in detecting silent MIs compared to patient recognition and extracardiac EKG detection tools.[67–70] The AngelMed Guardian System, therefore, should serve as a valuable option in the cardiologists' arsenal for many years to come.

Abbreviations

ACS, acute coronary syndrome; ASCVD, atherosclerotic cardiovascular disease; EKG, electrocardiography; MI, myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; S2D, symptom to door time; D2B, door to balloon time.

Disclosure

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