

Implantable cardiac monitors: State of the art

Abstract

Implantable Cardiac Monitor (ICM) provides continuous electrocardiographic monitoring in routine clinical practice in the identifications of infrequent arrhythmias. Studies have shown its efficacy in the evaluation of syncope, subclinical atrial fibrillation and post-ablation surveillance when compared to conventional external electrocardiographic monitoring. Sophisticated algorithms and miniaturization have increased the use of ICMs in clinical practice. An increased use ICM for the surveillance of arrhythmias has increased the workload required to analyze false positive transmissions. This necessitates an improvement in technology with the introduction of sophisticated algorithms to reduce the number of false-positive transmissions which will optimize the mismanagement and improve workflow and source utilization in device clinics. This review will summarize the recent development and clinical studies regarding the clinical utilities of ICMs.

Keywords: Implantable loop recorders • Atrial fibrillation • Screening • Accuracy • False-positive transmissions • Economic impact

Introduction

An Implantable Cardiac Monitor (ICM) is a subcutaneously implanted device used for ambulatory monitoring of arrhythmias in routine clinical practice [1]. Improved algorithms for the detection of arrhythmias and ease of implant procedures and wireless transmission have led to increased use of these devices. ICMs are commonly used for the detection of subclinical atrial fibrillation in patients with cryptogenic stroke, management of atrial fibrillation, syncope, and palpitations [2]. This review will summarize the recent development and clinical studies regarding the utilities of ICMs.

Current Guidelines

According to 2019 ACC/AHA/HRS guidelines, when external ambulatory monitoring is inconclusive, implantation of loop recorders is reasonable to optimize detection of subclinical AF in cryptogenic stroke (class IIa) [3]. Current recommendations favor the use of ICMs in monitoring the recurrence of AF after radiofrequency ablation to guide further therapy [4,5]. According to 2017 ACC/AHA/HRS guidelines, if initial evaluation of syncope is unclear and initial assessment suggests cardiac cause, ICM can be taken into consideration (IIa) [6]. In an evaluation of severe infrequent palpitations, when external EKG monitoring is inconclusive in documenting the underlying etiology, ICMs may be indicated according to European Society of Cardiology guidelines (IIa) [7].

Types of ICMs

There are four available ICMs currently. Medtronic (Minneapolis, MN, USA) manufactured Reveal™ XR that got approval in 2007. Over the course of years, significant improvements have been made in the implementation of several

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algorithms and particularly, the size of the device has significantly miniaturized such as Reveal™ LINQ. This device was approved for remote monitoring by managing physicians in 2020. BiMonitor™ (Biotronic, Berlin, Germany) was the second ICM introduced to clinical practice. Original BioMonitor was shaped like pacemakers and the subsequent generations BioMonitor II and III™ had extended antenna. With the availability of newer devices, BiMonitor™ is no more commercially available. Confirm Rx™ (Abbot, Abbot Park, IL, USA) is the third ICM that came into clinical practice. This was the first ICM compatible with smartphones and had BlueTooth technology. SharpSense technology is incorporated into the latest version of Confirm Rx™ and was approved in 2019. SharpSense technology was meant to reduce false-positive episodes. The latest ICM is LUX-Dx (Boston Scientific, Minneapolis, MN, USA). It resembles Confirm Rx™ and Reveal™ LINQ. Table 1 reports various features of ICMs.

ICM use in cryptogenic stroke

Cryptogenic strokes represent 10%-40% of all strokes. One of the most common uses of subcutaneous ICM is the detection of subclinical atrial fibrillation in cryptogenic stroke. Prolonged monitoring with ICMs has demonstrated that a substantial proportion of patients with cryptogenic stroke have subclinical atrial fibrillation. CRYSTAL AF trial studied Reveal XT™ devices in patients with cryptogenic stroke and identified subclinical atrial fibrillation in 8.9% vs. 1.4%, 12.1% vs. 2% patients by six and twelve months respectively when compared to control group (<0.001). This study was conducted at 50 centers across Europe, the US, and Canada [8]. Observational studies have shown the detection rates of 25% using ICMs in the evaluation of subclinical atrial fibrillation when compared to external monitoring which is reported to have a detection rate of 5%-20% in systemic reviews [9].

Table 1: Available implantable cardiac monitors and their features.

Feature	LINQ II	BioMonitor III	Confirm Rx	Lux Dx
Size (cm ³)	1.2	1.9	1.4	1.2
Battery life (years)	4.5	5.5	2	3
Atrial fibrillation algorithm	RR variability, P wave evidence score, Adaptive p-sense, Ectopy Rejection, AF evidence score	RR variability, RhythmCheck (to reject ectopic beats)	Markov Chain Variance, Sudden Onset and P-wave discrimination, sss	Dual Stage technology with Lorenz plot and verification step
Pause algorithm	Enhanced TruRhythm Smart Filter, Electrical noise Rejector, Loss of Contact Rejector	Signal dropout sensing system and histogram BioVector	SharpSense	Dynamic noise reduction, signal to noise ratio, signal loss
Minimum R-wave per manufacturer (mV)	0.2	1.7	0.1	0.3
PVC burden calculation	Yes	No	No	No
PVC burden calculation	Yes	No	No	No

ICM use in surveillance of AF post radiofrequency ablation

The ABACUS study evaluated the role of ICMs vs. conventional monitors in patients who underwent AF ablation and concluded that ICMs have a higher detection rate for arrhythmias when compared to conventional monitoring [5]. Voight, et al. studied the use of ICM in comparison to Holter monitoring in detecting new onset post atrial flutter and ablation. ICMs significantly enhances the detection of new-onset post atrial flutter ablation with a detection rate of 48% in comparison to 35% in the Holter monitor group [10]. Mittal, et al. also reported the importance of ICMs in post atrial flutter ablation surveillance in the detection of new-onset AF [11].

ICM use in the syncope

Clinical trials and observational studies have demonstrated the role of ICMs in the evaluation of transient loss of consciousness or syncope with an unknown initial evaluation and suspected due to arrhythmogenic etiology [12]. The diagnostic value of ICM is known to be superior to conventional ICMs [12-14]. The International Society of Syncope of Unknown Etiology (ISSUE) has reported the importance of ICM in patients with transient loss of consciousness [15,16]. PICTURE registry which comprised of data from 11 European countries evaluated the clinical outcomes of "Reveal" ICM in patients with recurrent syncope with diagnostic efficacy of 77% in patients with recurrent syncopal episodes.

ICM use in palpitations

In addition, ICMs are also have extended applications for the evaluation of palpitations [17]. The Recurrent Unexplained palpitations study concluded that ICMs are safe and more cost-effective when compared to conventional strategies in diagnosing patients with infrequent palpitations [18].

ICM use in the elderly patient population with frequent falls

ICMs are also noted to have diagnostic efficacy in assessing frequent falls in the elderly patient population. Bhangu, et al. studied the role of ICM in the elderly patient population with frequent falls. In this study, 70% of patients were identified with arrhythmias and 20% of this subset had treatable arrhythmia that could potentially have resulted in falls [19].

Device Data Collection

ICMs collect data by classifying it into four categories, bradycardia, tachycardia, pause, and atrial tachycardia/fibrillation. An episode of tachycardia is detected when the device detects a heart rate higher than the programmed rate of 230-age for a specified duration. Similarly, bradycardia is detected when the heart rate drops below a certain programmed rate for a certain period and is programmable. When no ventricular beats are noted for a certain programmable period, a pause is signaled. Similarly, atrial tachycardia and atrial fibrillation are diagnosed when specific criteria are met. Automatic algorithms based on Lorenz plots are used in the detection of atrial fibrillation. The thresholds for the detection of tachycardia, bradycardia, and pause can be adjusted and programmed.

Complications

The most complications are pain at site of implantation. Local pocket infection is another complication of ICM implantation and necessitates removal of the device. Moreover, poor R wave sensing may require moving the device to another location.

Discussion

Accuracy of arrhythmia detection

The fundamental principle for the detection of atrial fibrillation is the rate and irregularity of R waves. Device detected episode of atrial fibrillation after undergoing adjudication by device clinical personal or supervising physician is considered true atrial fibrillation. Devices can be programmed in a way that detects and notifies episodes of AF that last for a certain period. The minimum duration as the threshold for detection of AF varies across different ICMs; however, for the most part, an episode of AF lasting for at least 30 seconds meets the criteria and is taken into consideration.

The duration of AF that is clinically significant and needs to be treated is still under debate. Heart Rhythm Society identifies episodes of AF that lasts 30 seconds or more as clinically significant [20]. The sensitivity and specificity of ICM can be increased by changing the parameters for the length of episodes based on indications for ICM. Various algorithms are used to increase the accuracy of the detection of arrhythmias. As an example, the three-step algorithm is used by Reveal LINQ™ that helps improve diagnostic accuracy for the detection of atrial fibrillation. In the first step, the difference in the pattern of RR intervals is computed to score the AF evidence score every 2 minutes. This is followed by the detection of “p” wave evidence scores. The last step is to assess for the presence of “p” wave during “RR” irregularity intervals as evidence of ectopy, sinus arrhythmia and optimizes the detection of AF with higher sensitivity [21]. Reveal LINQ system used TruRhythm detection software, which was released in 2017, and equipped with a fifth-generation algorithm for atrial fibrillation that adapts to “P” wave over the course of time, a second sensing filter for analyzing rhythms in bradyarrhythmias or pauses and streamlines review and reporting that reduced the frequency of false-positive episodes [11,21]. A higher rate of false-positive detection in earlier studies led to further enhancement in algorithms of subcutaneous ICMs [5,22,23]. As an example, a reduction in false positive rate to 0% was noted in Confirm Rx™ after the introduction of new algorithms in a subset of patients receiving ICM for various indications [24]. Lux Dx™ ICM use a two-step algorithm in which two-minute windows analyze variability in RR intervals and heart rate which is followed by the application of additional criteria to rule out under or over sensed episodes. The BioMonitor III™ algorithm for AF assesses the variability in RR intervals and the variability must occur for a programmed specific period to identify it as a positive episode. Ectopic beats are rejected through its RhythmCheck technology. Similarly, Confirm Rx™ uses a similar AF algorithm in which a window of 64 beats is evaluated for variability in RR interval and the onset of the episode whether slow or fast. SharpSense technology is used to monitor for the presence or absence of p waves. The absence of P waves signals the storage of episodes by the device. SharpSense Technology software used extra discriminating factors to improve accuracy and enabled review of previous 30 seconds for p wave detection. Customized thresholds created by dynamic evaluation of multiple R and P waves improve the sensitivity to detect true bradyarrhythmia and secondary thresholds created through analysis of P and R waves during the previous 6 seconds improve sensitivity to true pause episodes [25].

Studies evaluation comparative efficacy and false-positive transmission rates

Ip, et al., for the first time, studied the comparative efficacy and accuracy of data transmission and arrhythmia detection with the latest software of Reveal LINQ (Medtronic, Dublin, Ireland) and Confirm Rx (Abbot, Sylmar, CA) which are routinely used in clinical practice [26]. Both ICMs have introduced an enhanced algorithm to reduce false positive detection rates and can remotely be monitored. In this randomized clinical trial, ICMs were programmed with the same parameters in all patients. Bradycardia was defined with heart rate ≤ 40 per minute, arrhythmic events were defined as pause ≥ 3 seconds, tachycardia with heart rate 150 per minute, and AF episodes lasting at least 6 minutes were taken into consideration. This was a single-center study on 61 patients over 7.1 ± 3.5 months making a total of 3510 events. Transmission time for all events (448 ± 271 vs. 610 ± 515 minutes, $P=0.02$) and patient activated triggers (24 ± 103 vs. 475 ± 426 minutes, $P<0.0001$) was significantly shorter in Confirm Rx group. Moreover, the total number of events was higher in the Confirm Rx group (25.5 ± 45.6 vs. 0.9 ± 1.1 events per patient-month, $P<0.01$). Confirm Rx group was noted to detect true arrhythmic episodes sooner and

with a higher percentage of diagnosed patients during follow-up of 6 months. Patient average true positive detection rates were not statistically significant in the two groups for AF (52% vs. 38%); bradycardias (67% vs. 59%); tachycardia (81% vs. 94%) and pause (24% vs. 20%) comparing Reveal LINQ vs. Confirm Rx respectively (Table 2). It was concluded that Confirm Rx had a shorter transmission time, higher event detections, shorter duration to the diagnosis of true arrhythmias leading to a higher percentage of diagnosed patients while the accuracy of arrhythmia detection remained suboptimal in both systems. The differences in detection were attributed to faster transmission with Bluetooth technology and arrhythmia algorithms in Confirm Rx group. In addition, all arrhythmic events are transmitted from Confirm Rx group in contrast to the Reveal LINQ system which audits the events and prioritizes ventricular episodes and longest AF episodes followed by manual transmission to evaluate the remaining events stored in the device. This study reported high false-positive rates in both ICMs (62% in Confirm Rx and 48% in Reveal LINQ). A high false-positive rate was attributed to premature beats, duplicate counting of P waves, T waves, and noise after adjudication of false-positive AF events [26].

Table 2: Baseline characteristics and detection rates in Confirm Rx and Reveal LINQ systems.

Variable	Confirm Rx (n=70)	Reveal LINQ (n=72)	P value
Age	58 ± 17	63 ± 13	0.09
Male %	48.6	41.6	0.97
Indication for implant			
Stroke, n	48	50	
0.24	Yes	Yes	Yes
Palpitation, n	6	4	
Syncope, n	16	18	
Detection rates in 61 patients over 7.1 months			
Number of transmitted arrhythmic events, per patient month	25.5 ± 45.6	0.9 ± 1.1	<0.01
Event transmission time for all events, minutes	448 ± 271	610 ± 515	0.02
Patient activated events, per patient	6.3 ± 3.8	1.8 ± 1.6	<0.0001
Time from activation to data transmission, minutes	24 ± 103	475 ± 426	<0.0001
TP, AF detection rates, %	52	38	0.5039
TP, Bradycardia detection rate, %	67	59	0.7857
TP, Pause detection rate, %	24	20	0.6471
TP, Tachycardia detection rate, %	81	94	0.4633
Abbreviations: TP: True Positive; AF: Atrial Fibrillation			

Afzal, et al. also reported high false-positive transmission ranging from 46% to 86% depending on the indication for ICMs. Data over a period of 4 weeks included remote transmissions using Reveal LINQ system implanted for surveillance of atrial fibrillation, cryptogenic stroke, and syncope. It reported a false-positive transmission rate of 46%, 86%, and 71% in patients with atrial fibrillation, cryptogenic stroke, and syncope respectively. Under sensing and signal drop were primary causes for high false-positive rate in scheduled transmission while premature atrial and ventricular ectopic beats were primary reasons for false-positive events in alert transmissions. The incidence of false-positive transmission rate was similar in Reveal LINQ with and without TruRhythm technology (P 0.21). They concluded that it requires considerable commitment and time from device clinic staff and the electrophysiologists to adjudicate the transmissions and avoid potential errors in diagnosis and management [27].

Chorin, et al. retrospectively studied diagnostic yield and accuracy of Reveal LINQ (4th generation) and fifth-generation device with TruRhythm technology in patients with cryptogenic stroke. They reported AF in 12% of patients over a period of 28 ± 12 months. After adjudication by an electrophysiologist and device technician, false-positive rates ranging from 84% to 96% were detected depending on the presence or absence of TruRhythm technology and attributed high false-positive rates to premature atrial beats in Reveal LINQ system and oversensing of T waves in TruRhythm LINQ system. This study noted a false-positive rate for detection of AF in cryptogenic stroke as high as 84% necessitating interpretation of recordings by experts to ensure accurate diagnosis and avoid mismanagement [28].

Resource utilization and economic impact of ICMs

Afzal, et al. studied the economic impact and resource utilization of rhythm monitoring with ICMs. Consecutive 1,457 transmissions from 1,811 ICMs were studied over a period of 4 weeks. The average time spent per transmission adjudication by device clinic personal was 15 ± 6 minutes which totaled 364 hours over a period of 4 weeks, which cumulated to a salary of \$12000 U.S. dollars. The average time spent per transmission adjudication by an electrophysiologist was 1.5 ± 1 minutes which totaled 37 hours over a period of 4 weeks, which cumulated to a salary of \$9,600 U.S. dollars. 35% of transmissions were repeatedly from the same patients which resulted in no additional reimbursement. About 50% of transmissions were false positive, out of which, 60% of transmissions were “Alert” and 49% of transmissions were from “full downloads” (p 0.04). They also showed that institutional custom programming was compared to nominal programming by

manufacturers, a reduction in false-positive transmission (55% in “Alert” vs. 16% in “Full downloads”, p 0.01) was noted [29].

Current and Future Studies

LOOP study is an event-driven randomized control trial that aims to determine the risk of stroke and systemic arterial thromboembolism in atrial fibrillation episodes lasting for ≥ 6 minutes detected by ICM and treated with anticoagulation. Rigshospitalet, Denmark is sponsor for this trial. The study included 6000 participants who are randomized in a 3:1 fashion to the control group (4500) vs. the ICM group which receive treatment with LOOP study is an event-driven randomized control trial that aims to determine the risk of stroke and systemic arterial thromboembolism in atrial fibrillation episodes lasting for ≥ 6 minutes detected by ICM and treated with anticoagulation. Rigshospitalet, Denmark is sponsor for this trial. The study included 6000 participants who are randomized in a 3:1 fashion to the control group (4500) versus the ICM group which receive treatment with anticoagulation in case AF is detected. The study included patients older than 70 years and have more than 1 risk factor for strokes such as hypertension, diabetes, heart failure, or history of stroke. This trial was planned to continue until 279 adjudicated primary events have occurred. The study is complete, and results are awaited.

University of Pittsburg will initiate a trial this year i.e., “Arrhythmia Detection after Myocardial Infarction trial (AID-MI)”. AID-MI is an Abbott-funded randomized control trial, sponsored by the University of Pittsburg Medical Center. It is aimed to assess whether patients with acute myocardial infarction should receive or not receive Confirm Rx ICM. This trial aims to study 200 patients post MI at 10 sites in the United States, randomized based on left ventricular ejection fraction and followed for two years. The primary endpoint for this trial is 90 days rate of rhythm findings in monitored and control arms that will lead to changes in management.

Future Perspectives

The growing use of ICMs for the detection and surveillance of arrhythmias is putting a significant workload due to increased adjudication required with high false-positive transmissions [30]. Afzal, et al. reported average time consumed to review one transmission was about 30 to 45 minutes [27]. This necessitates an improvement in technology with the introduction of sophisticated algorithms to reduce the number of false-positive transmissions which will optimize the mismanagement and improve workflow and source utilization in device clinics. Moreover, customizing the programs to turn off arrhythmias that are clinically irrelevant or increasing the duration of arrhythmia may help increase the

specificity [29]. Moreover, the clinical outcomes resulting from differential false-positive transmissions need to be studied. ICM use is safe with reported infection rate of 1%-2% [30].

Conclusion

ICM is a valuable tool for the detection of arrhythmia and has been shown in various clinical trials in the management of patients with atrial fibrillation, unexplained syncope, and cryptogenic stroke. However, the accuracy and specificity of arrhythmia detection especially atrial fibrillation is still suboptimal. Further enhancement in the detection algorithm is needed to broaden the clinical utilities of ICM.

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