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The implantable cardiac monitor in heart failure patient: a possible new indication?

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Implantable cardiac monitors (ICMs) have found increasing use in clinical practice over the years, proving, when used in high-risk populations, to facilitate the diagnosis of bradyarrhythmias and tachyarrhythmias requiring treatment. Experience with heart failure patients undergoing pacemaker (PMK) or implantable defibrillator (ICD) implantation, which allow for continuous electrocardiographic monitoring and transthoracic impedance assessment, has made it possible to identify predictors of heart failure flare-ups. In this context, the use of telemonitoring has been shown to ensure better management of patients with heart failure. These benefits cannot be assessed to date in patients with heart failure and left ventricular ejection fraction (LVEF) > 35% who have no indication for PMK or ICD implantation. This population has been shown to have a significant incidence of ventricular arrhythmias and bradyarrhythmias. In addition, a significant number of cerebrovascular events are observed in this population, largely attributable to the high incidence of atrial fibrillation (AF). In this population, the occurrence of AF has also been shown to have a negative impact on patients' prognosis; at the same time, a rhythm control strategy has been shown to be more beneficial in this area than a rate control strategy. Studies also suggest arrhythmias have a negative impact on the cognitive status and quality of life of heart failure patients. These reasons could justify the implantation of ICMs equipped with telemonitoring systems in heart failure patients. The information provided by the monitoring system, if properly managed, could bring benefits in terms of prognosis and quality of life along with a reduction in economic costs. We will try here, by answering a few questions, to assess whether there is an indication for ICM in heart failure, which patients should be candidates and how these patients should be managed.

Introduction

Over the years, implantable cardiac monitors (ICM) have found increasing use in clinical practice.

These devices have been progressively miniaturized and improved, especially by implementing the possibility of remote monitoring. This has reduced the time needed to make a diagnosis, improved patient compliance and changed the follow-up strategy with a potential reduction in healthcare costs. However, the use of such devices must always be carefully evaluated.

Generalizing, we can say that the appropriate use of an ICM to be should fulfill these conditions:

(1) There is a reasonable probability that the 'X' event we are looking for will occur within the monitoring timeframe.
(2) Early identification of this 'X' event allows behavioural/therapeutic measures to be taken that may influence the patient's prognosis and/or quality of life

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(3) The patient does not have another cardiac implantable electronic device (CIED) that can provide the same information.
(4) There are no equally effective non-invasive methods that can be used to achieve our goal.

Therefore, taking these principles as a reference, we will try to answer some questions to evaluate whether there may be an indication to use the ICM in the decompensated patient.

Why?

Heart failure is one of the most common chronic diseases in the general population. This syndrome is characterized by frequent phases of exacerbation in a context of chronic, often labile, balance. To better define the prognosis and risk of worsening heart failure, various strategies have been hypothesized to follow the patient even outside the outpatient clinic and independent of frequent hospitalizations. The possibility of remote monitoring with devices such as implantable cardioverter defibrillator (ICD), cardiac resynchronization therapy (CRT) has been evaluated to reduce hospitalizations when the patient has an indication to have these devices implanted. In addition to the monitoring of arrhythmias and possible therapeutic intervention, these devices also have the ability to use parameters such as an increase in mean heart rate and respiratory rate (sensed by the electro-catheters) to predict a deterioration in a patient's clinical condition that could lead to hospitalization. This kind of monitoring therefore gives the opportunity of early therapeutic intervention and consequently outpatient and/or home management without the need for hospital care, which equals cost savings and a positive impact on the patient's quality of life in addition to reducing the chance of adverse events (e.g. infections) caused precisely by frequent hospitalization.[1]

In order to improve haemodynamic monitoring, devices that can provide information on deterioration with possible fluid accumulation and increased filling pressures in patients with heart failure have also been created, such as the Cardio MEMS device which is implanted in the pulmonary artery.[2] By measuring changes in pulmonary artery pressure, this device is able to use this parameter as an early indicator of haemodynamic deterioration for early optimization and titration of heart failure therapy. Regarding the monitoring of arrhythmic events, several studies have shown it is equally important to assess the presence of supraventricular and ventricular arrhythmias. There are several arrhythmic parameters that can provide prognostic information about the worsening clinical status of the heart failure patient such as heart rate variability, atrial fibrillation (AF) burden, mean ventricular rate during AF and mean nocturnal rate.[3] Another fundamental point is that the ability to detect these events can then have a practical implication in the early decision to implement diagnostic-therapeutic choices. Remote monitoring by devices such as ICD or CRT is provided only for those who have other indications for implantation of such devices, which are usually provided for subjects with heart failure with reduced ejection fraction (left ventricular ejection fraction (LVEF) <35% is the main indication for implantation considered by the different guidelines) and less frequently for patients with mid-range or preserved ejection fraction. On the other hand, simple ambulatory monitoring with 24-hour Holter ECG was demonstrated by Teerlink *et al*.[4] (who studied the impact of non-sustained ventricular arrhythmias on the prognosis heart failure patients) to not show significant value in predicting the risk of sudden cardiac death, probably due to the limited monitoring period. In our experience, non-invasive rhythm monitoring systems are also limited by frequent measurement errors and poor patient compliance. These systems also allow us to monitor EKG only a few minutes a day.[5]

The potential role of implantable loop recorder (ILR) was investigated in a small sample size study by Kort *et al*. in which 13 of the 30 patients recruited in the study underwent a change in therapeutic strategy due to the data derived from the ILR (eight patients had developed subclinical AF and one patient required implantation of a PMK).[6]

Different kind of arrhythmias detected and their clinical implications

One of the fundamental indications for the implantation of a device that recognizes arrhythmic events is the recording of the heart rhythm for a time adequate to allow the possibility of detecting them during the monitoring itself. Therefore, some authors have proposed utilization of the implantable loop recorder in patients with heart failure mainly with mid-range or preserved ejection fraction for arrhythmic risk stratification and thus with an intention of prognostic evaluation. In 2019 Adabag *et al*. in an attempt to identify a risk score that included six variables (age, sex, myocardial infarction, diabetes mellitus, bundle branch block, N terminal pro Brain Natriuretic Peptide) to better define the risk of sudden cardiac death at 5 years, demonstrated that sudden cardiac death was the most common single cause of death in patients with Heart failure and preserved ejection fraction (HFpEF).[7]

In the same year Gutierrez et al. showed, by applying a 14-day ambulatory monitoring device in 40 patients with HFpEF, that there were 32.5% of patients with episodes of non-sustained ventricular tachycardia (NSVT), 5.0% with paroxysmal AF and 80.0% with episodes of supraventricular tachycardia during the monitored period.[8] All patients had premature ventricular complexes (PVC) with 7.5% having a PVC burden that exceeded 5%. Furthermore, Ash *et al*. (on the assumption that ventricular tachycardias could explain a large proportion of SCD events in patients with HFpEF) evaluated the prevalence of NSVT in patients over a follow-up period of 3 years, demonstrated that 44.7% of patients had ventricular arrhythmias registered at device check. In patients with a presence of ventricular tachycardias during the follow-up, there was a trend toward increased mortality (18.4 vs. 8.5%) in respect of those without.[9]

More recently the VIP Study[10] evaluated the incidence of non-sustained ventricular tachycardia in patients with preserved or a mid-range ejection fraction. In this study, 113 patients underwent a complete evaluation by imaging technique and 24-H Holter Monitoring and were then investigated through continuous rhythm monitoring with an implantable loop recorder. Patients had a scheduled visit every six months for ILR interrogation for a maximum

period of 2 years. Despite the low incidence of ventricular tachycardia, the ILR proved to be a more reliable method compared to 24 Holter monitoring in identifying patients with ventricular tachycardia (almost 10% higher). In contrast to what was expected, the ventricular arrhythmias were not associated with an increased risk of hospitalization or mortality. However, the detection rate of ventricular arrhythmias was meaningful and the implantation of ILR demonstrated an ability to uncover AF and bradyarrhythmias (that have an impact on heart failure patients' prognosis) with a low incidence of adverse events from the implantation procedure.

When investigating the incidence of stroke and myocardial infarction in patients with heart failure, Fonarow *et al*. showed that heart failure patients with preserved ejection fraction had a higher incidence of AF than patients with reduced ejection fraction, which may also be attributable to the higher mean age and higher proportion of female patients. Even in the absence of a direct proportionality between the incidence of AF and stroke in this group of patients, it is clear that the early detection of AF during the follow-up of patients with HF may be an effective strategy for the prevention of cardioembolic stroke.[11]

As early as in 2006, in an analysis derived from the CHARM study, which enrolled patients with different ejection fractions, the incidence of AF over a follow-up of 3 years was evaluated. AF was a major predictor of adverse outcome in terms of morbidity, mortality, and adverse cardiovascular events. It is important to emphasize that the relative risk of major adverse outcome, such as cerebrovascular events and mortality due to AF, was greater in patients with preserved ejection fraction than in those with reduced ejection fraction (HR 1.72 vs. 1.29).[12] Highlighting the importance of rhythm monitoring not only to detect events that could be significant in terms of prognosis but also to improve the therapeutic strategy of patients with arrhythmic events.

In 2019, Kelly *et al*. showed that a rhythm control strategy compared to a rate control strategy was associated with a lower risk of mortality (30.8% vs. 37.5%, *P*-value $<$ 0.01) in two comparison groups of patients with HFpEF.[13] Therefore, using continuous monitoring to aid the early diagnosis of AF, even if silent, could improve the timing of the start of a rhythm control strategy. Recently it was demonstrated that the prevalence of subclinical cerebral infarctions (SCI) detected by cerebral magnetic resonance examination in patients with HFpEF and no anamnestic history of AF (29.3%) was comparable to that of patients with known AF with HFpEF (24.5%) or not (23.5%) and was higher compared to patients neither with a diagnosis of HFpEF nor AF (17.3%). As expected these data also had clinical implications, for example, patients with HFpEF and evidence of SCI had lower cognitive score compared to patients without SCI.[14] The authors of the study concluded that these observations suggest that AF may be extensively underdiagnosed in this group of patients, likely due to its paroxysmal nature; with even seemingly silent AF having a clinical impact on patients' status.

In a large meta-analysis evaluating the prevalence of dementia in patients with AF,[15] it was shown that over 8 years of follow-up, patients with AF were significantly more likely to develop dementia than patients without AF. Numerous other studies have confirmed that patients with AF have a lower Modified Mini Mental State Examination score and develop dementia earlier than patients in constant sinus rhythm. Several hypotheses have been put forward to explain the pathophysiology of these correlations. In particular, an association has been suggested between dementia and haemodynamic alterations such as the irregularity of the R–R interval. An elevated mean frequency is often associated with low blood pressure that could contribute to cerebral hypoperfusion, especially of those areas most sensitive to ischaemic damage such as the hippocampus. Frequent and undetected ischaemic stroke or even microbleeds due to the anticoagulant therapy could also contribute. In addition, the pro-inflammatory state, oxidative stress, endothelial dysfunction, and even atrial remodelling with an accumulation of fibrosis and proteinaceous material typical of the pathophysiology of AF could share and anticipate mechanisms that lead to cognitive decay, in a manner similar to known pathologies such as Alzheimer's disease.[16] There is less evidence of the role of bradyarrhythmias in the development of cognitive impairment. Some small trials have shown that a likely improvement in cerebral perfusion after PMK implantation for symptomatic bradycardia significantly improved patients' cognitive function. However, this conclusion was not consistently confirmed or supported by other studies.

Economic considerations

The use of remote monitoring from home, which allows for adequate and early diagnosis and consequently prevention, is certainly also an economic issue. If we consider the data published in the ARNO DATABASE Italian registry,[17] we can clearly see that the costs of the decompensated hospitalized patient (with a hospital stay that on average exceeds 10 days) equates to a total of 550 million euros spent by the Italian national health system annually. The per patient annual expenditure is 11 800 euros, 85% of which is solely for hospitalization costs. The cost of a re-hospitalization is almost double that of the first admission (over 7000 euros compared to about 4500 for the first admission). Therefore, even in purely economic terms, the potential cost savings from implementing a strategy aimed at avoiding the frequent re-hospitalization of decompensated patients are obvious.

To whom and when?

Heart failure patients who may benefit from the implementation of the loop recorder are clearly those in which there is no indication for an ICD or PMK.

Among these patients, according to what has been previously expressed, ICM use may provide particular advantages in patients not taking anticoagulant therapy and have no contraindications to its use.

In addition, it is likely that patients with atrioventricular or intraventricular conduction delays may represent a category in which ICM-based management has a major advantage, as well as those in which beta-blocking therapy is indicated or those with evidence of myocardial scar.

In the heart failure patient, the most appropriate time for ICM monitoring may be when the patient has reached a clinical status that may reasonably avoid indication for

other types of CIEDs. The presence of episodes of palpitation in the preceding six months to ICM implant also increases the possibility of detecting clinically relevant arrhythmias.

What and where?

Regarding the choice of device type we believe that the possibility of remote monitoring is crucial in devices being used in decompensated patients. In addition to the detection of arrhythmic events, the ability to provide information on heart rate variability and congestion status are particularly useful tools in this area. Information from an ICM-based monitoring system will be useful if it is managed by the staff caring for the patient. Therefore the 'place' where this type of indication can be of real benefit is in the heart failure clinic.

How?

In the field of heart failure monitoring, ICM programming and alert management require a tailor-made approach to the individual patient. To prevent worsening of chronic heart failure we also believe it necessary to evaluate transmissions within 7 days in order to provide a sufficiently timely therapeutic response.

New perspectives—our proposal

Experiences with loop recorder monitoring of patients with heart failure are currently limited and related to a small number of patients.

These studies have shown the ability of loop recorders to detect a high number of arrhythmic events requiring therapeutic modifications in these subjects, however, these studies, as designed, do not allow the prognostic impact of this monitoring strategy to be assessed.

In order to clarify the potential effects of loop recorder-based telemonitoring in patients with heart failure, our group proposes a case-control study: 'Evaluation of a proactive clinical management and early diagnosis of arrhythmias in patients with heart failure and non-severely reduced left ventricular function through a telemonitoring system: a prospective randomized clinical trial. VASCO STUDY'

This will be a multicentre, international, prospective, randomized, non-profit study.

The study will enrol patients with heart failure, LVEF > 40% who report episodes of palpitations.

The exclusion criteria are: Pregnancy, Medical contraindications for ILR implantation, Patients with PMK/ICD or with Indication for ICD/PMK implantation, cardiovascular events/myocardial revascularization in the previous three months, patients already on oral anticoagulant treatment, Patients who do not want to use the telemonitoring system, presence of other recognized indications to ILR (Unexplained syncope, cryptogenic stroke/TIA, Transient loss of consciousness and recurrent falls)

Going into more detail about the objectives, we want to evaluate the benefits of a ILR-based remote monitoring management compared to standard practice in patients with a high risk of cardiac arrhythmias, heart failure, and LVEF > 40% in detecting clinically significant events.

We also want to compare ICM-based management vs. conventional management in terms of the incidence rate of a composite endpoint of arrhythmic events, risk reduction of a composite cardiovascular endpoint, and quality of life.

In addition, we want to evaluate the cost-effectiveness of ICM-based remote monitoring management vs. standard practice in this population.

Conclusions

Decompensated patients certainly represent a population with a high incidence of arrhythmic events. Even in those who do not have an indication for an ICD or pacemaker, continuous electrocardiographic monitoring together with information on congestion status, if appropriately collected and managed, can reasonably be expected to bring benefits in terms of prognosis and quality of life. Comparative studies are needed to quantify these benefits compared to standard management and to measure their impact in economic terms. Our group's proposal goes in this direction.

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Data availability

No new data were generated or analysed in support of this research.

References

1. Hawkins NM, Virani SA, Sperrin M, Buchan IE, McMurray JJV, Krahn AD. Predicting heart failure decompensation using cardiac implantable electronic devices: a review of practices and challenges. *Eur J Heart Fail* 2016;**18**:977–986.
2. Adamson PB, Abraham WT, Warner Stevenson L, Desai AS, Lindenfeld J, Bourge RC *et al*. Pulmonary artery pressure-guided heart failure management reduces 30-day readmissions. *Circ Heart Fail* 2016;**9**: e002600.
3. Monzo L, Schiariti M, Calvisi PF, Bonfiglio S, Luštrek M, Puddu PE. Association of patient-reported outcomes and heart rate trends in heart failure: a report from the chiron project. *Sci Rep* 2020;**10**:576.
4. Teerlink JR, Jalaluddin M, Anderson S, Kukin ML, Eichhorn EJ, Francis H *et al*. Ambulatory ventricular arrhythmias in patients with heart failure do not specifically predict an increased risk of sudden death: PROMISE (prospective randomized milrinone survival evaluation) investigators. *Circulation* 2000;**101**:40–46.
5. Martino AM, Cicogna F, Palozzi G, Tota C, Monzo L, Mennuni S *et al*. Clinical and economic impacts of remote management of heart failure with preserved ejection fraction: preliminary results of a single center experience. *Eur J Heart Fail* 2020;**22**:2–415.
6. Kort RSS, Tuininga YS, Bosker HA, Janssen M, Tukkie R. Telemonitoring with an implantable loop recorder in outpatient heart failure care: one year follow-up report from a prospective observational Dutch multicentre study. *Neth Heart J* 2019;**27**:46–51.
7. Adabag S, Langsetmo L. Sudden cardiac death risk prediction in heart failure with preserved ejection fraction. *Heart Rhythm* 2020;**17**: 358–364.
8. Gutierrez A, Jerry Ash J, Akdemir B, Alexy T, Cogswell R, Chen J *et al*. Nonsustained ventricular tachycardia in heart failure with preserved ejection fraction. *Pacing Clin Electrophysiol* 2020;**43**:1126–1131.

9. Ash J, Akdemir B, Gutierrez A, Chen J, Adabag S. Ventricular tachycardia is a common arrhythmia among patients with heart failure with preserved ejection fraction. *Circulation* 2019;**140**:A11658.
10. van Veldhuisen DJ, van Woerden G, Gorter TM, van Empel VPM, Manintveld OC, Tieleman RG *et al*. Ventricular tachyarrhythmia detection by implantable loop recording in patients with heart failure and preserved ejection fraction: the VIP-HF study. *Eur J Heart Fail* 2020; **22**:1923–1929.
11. Fonarow GC, Peterson ED, Greenberg B, Berger JS, Lefebvre P. Stroke and myocardial infarction risk among newly diagnosed heart failure patients with reduced, borderline, and preserved left ventricle ejection fraction. *J Cardiac Fail* 2017;**23**:S29–S30.
12. Olsson LG, Swedberg K, Ducharme A, Granger CB, Michelson EL, McMurray JJV *et al*. Atrial fibrillation and risk of clinical events in chronic heart failure with and without left ventricular systolic dysfunction: results from the candesartan in heart failure-assessment of reduction in mortality and morbidity (CHARM) program. *JACC* 2006;**47**:1997–2004
13. Kelly JP, DeVore AD, Wu J, Hammill B, Sharma A, Cooper LB *et al*. Rhythm control versus rate control in patients with atrial fibrillation and heart failure with preserved ejection fraction: insights from get with the guidelines-heart failure. *J Am Heart Assoc* 2019;**8**: e011560.
14. Cogswell RJ, Norby FL, Gottesman RF, Chen LY, Solomon S, Shah A *et al*. High prevalence of subclinical cerebral infarction in patients with heart failure with preserved ejection fraction. *Eur J Heart Fail* 2017;**19**:1303–1309.
15. Santangeli P, Di Biase L, Bai R, Mohanty S, Pump A, Cereceda Brantes M *et al*. Atrial fibrillation and the risk of incident dementia: a meta-analysis. *Heart Rhythm* 2012;**9**:1761–1768.
16. Dagres N, Chao TF, Fenelon G, Aguinaga L, Benhayon D, Benjamin EJ *et al*. European Heart Rhythm Association (EHRA)/Heart Rhythm Society (HRS)/Asia Pacific Heart Rhythm Society (APHRS)/Latin American Heart Rhythm Society (LAHRS) expert consensus on arrhythmias and cognitive function: what is the best practice? *Europace* 2018; **20**:1399–1421.
17. Maggioni AP, Orso F, Calabria S, Rossi E, Cinconze E, Baldasseroni S *et al*. The real-world evidence of heart failure: findings from 41 413 patients of the ARNO database. *Eur J Heart Fail* 2016;**18**:402–410.