Section A-Research paper
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A review on the role of pacemakers used to induced hypertension control.

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Abstract:

The control over hypertension has been a greater challenge in the health care sector. Lack in hypertension control accounts to a lot of reasons. The prime reason accounts to the lack of adherence to the medication regime. This review article mainly discuss on the factors on which leads to the medication non adherence. Usually the complex medication schedule sites out to be the prime reason in the control of hypertension. Medication regime that has more than 3 pills have the least rate of adherence and patients who follow 1 pill regiment have higher rates of adherence.

This non ability to adhere to the medications were the reasons why this research on using pacemaker to control hypertension. The pacemaker uses a particular algorithm to control hypertension by regulating the AV pumping interval.

A ModeratoTM pulse generator that administers PHC therapy was implanted in patients who were recommended for dual-chamber pacing and had office systolic blood pressure (oSBP) >150 mm Hg despite stable medication therapy.

A month was spent running the trail at a regular pace. PHC was activated and patients with oSOP (Office Systolic Blood Pressure) > 140 mm Hg were admitted to the study.

The 3-month therapy phase, which comprised PHC therapy, was opened to patients who during the Run-In phase met the blood pressure standards for inclusion (oSBP >140 mm Hg at 2 and 4 weeks). The day PHC therapy began (time=0) was the trial's start date.

The co-primary efficacy end objectives were changes in 24-hour ambulatory systolic blood pressure and oSBP between baseline and three months. As a safety measure, bad incidences were monitored.

In New Hope, Pennsylvania, BackBeat Medical manufactures the Moderato System, a dual-chamber, rate-responsive pacemaker implantable pulse generator (IPG). A sequence of variable-timed, alternately shorter (20–80 ms) and longer (100–180 ms) atrioventricular intervals are used to pace the heart using PHC algorithms.

Key words: Hypertension, Medication non adherence, Ambulatory blood pressure, Office systolic blood pressure, PHC and Moderato^{TM}.

Introduction:

Since its first introduction in the 1960s, the pacemaker has grown to be a marvel of modern invention. When the heart beat becomes sluggish or misses a beat, pacemakers are utilized to control the heartbeat. Therefore, this pacemaker sends out an impulse to get the heart beating normally. [1]

Pacemakers' features and specifications changed over time. There are different kinds of pacemakers. Depending on your symptoms and the particular heart problem you have, a pacemaker may be necessary. We share our recommendations with you after performing our diagnostic assessment so you may select the best pacemaker for your requirements. [2]

1. **Single Chamber Pacemaker:**

With this type of pacemaker, one lead is used to connect the pulse generator to one of the chambers of your heart. To regulate patients' heartbeat pacing, we most frequently attach the lead to your right ventricle while using a single-chamber pacemaker (lower heart chamber). Depending on your symptoms and the type of pacing you require, the lead is attached to your right atrium (upper heart chamber) to induce pacing there. [3]

2. **Dual Chamber Pacemaker:**

The right atrium and right ventricle, the two chambers on the right side of your heart, are connected by two leads that are part of this device. The doctor configures the dual-chamber pacemaker to regulate the rate at which each chamber contracts.

With the aid of this pacemaker, the two chambers contract and relax at the proper rate. The contractions allow for efficient blood exchange between the right atrium and right ventricle. [4]

3. **Biventricular Pacemaker:**

This pacemaker, also known as a cardiac resynchronization treatment (CRT) device, has three leads linked to the right atrium and both ventricles. Patients with arrhythmias linked to progressive heart failure are treated with the biventricular pacemaker.

The left and right ventricles do not always pump in unison in persons with heart failure. The biventricular pacemaker is programmed by our experts to synchronise the ventricle contractions so that they both pump at the same time. [4]

Your heart pumps blood more effectively when the ventricles are coordinated, which can lessen the symptoms of heart failure. Because it resynchronizes the ventricles' pumping function, the procedure is referred to as cardiac resynchronization therapy. [5]
Since pacemakers are surgically implanted devices, they must pass numerous safety tests, and patients must also go through numerous examinations to determine whether they are eligible for pacemaker installation. [5]

Early evidence of device based therapy for controlling hypertension:

Renal denervation:

2009 saw the publication of the first case study of catheter-based RDN (renal denervation) in a patient with chronic resistant hypertension (mean office BP, 161/107 mmHg). The patient was a male patient, age 59. 13 The patient's blood pressure stabilised to 127/81 mmHg at twelve months after bilateral treatment with a highly specialised radiofrequency RDN device, and renal norepinephrine spillover from the left and right kidneys also decreased (by 48% and 75%, respectively), indicating successful renal nerve ablation. The clinical development of catheter-based RDN might be seen as beginning with this clinical example, which generated a lot of interest in this novel approach. [6][7]

Device-based hypertension treatment is a supplement to, and maybe an alternative to, traditional lifestyle changes combined with antihypertensive medications with the purpose of achieving and maintaining optimal blood pressure (BP) management. Current device-based hypertension therapies include cardiac pacemaker-mediated hypertension treatment, baroreceptor activation therapy, endovascular baroreflex amplification, and endovascular catheter-based renal denervation (RDN). Clinical trials examining various cutting-edge technologies are also still being conducted. [8]

Despite not meeting its primary effectiveness target, the SYMPLICITY HTN-3 randomised, blinded, sham-controlled trial did confirm renal denervation's safety (RDN). RDN research from the past has demonstrated that blood pressure can be dramatically and permanently decreased. [9,10]

Baroreflex activation therapy:

A tool employed in the baroreflex activation treatment study for the treatment of hypertension was the CVRx Rheos system. This device comprises of two carotid arteries that are joined together at the level of the carotid sinus with implanted electrodes. [11,12]

The trial included patients who were on more than three anti-hypertensive drugs and had refractory, uncontrolled hypertension. According to the trail, there was a significant drop in workplace SBP and office DBP within three months. Nevertheless, there was no discernible reduction in ambulatory blood pressure (AbBP). [13] [14]

Later, a six-month long sham controlled randomised research with 265 patients with drug-resistant hypertension was conducted. The protocol-specified objectives for acute efficacy and procedural safety, however, were not met by the experiment. As a result, the USFDA was compelled to refuse to approve the device. [15] [16]

Endovascular Baroreflex amplification:

First human study that was uncontrolled and unbound was "The controlling and lowering of blood pressure with the Mobius HD." On 30 patients, the study was intended to evaluate the device's effectiveness and safety. [17]

Here, detecting the incidence of major side effects for six months, including any unexpected side effects, was the main goal. [18,19]

The ambulatory blood pressure (AbBP) and office blood pressure variations during a 24-hour period, coupled with the use of anti-hypertensive drugs, were the secondary end points. [19]

No strokes or transient ischemic episodes were reported, although 5 patients had substantial side effects. The anti-hypertensive drugs were decreased during a six-month period, but lengthier safety and efficacy data were not made public. [19]

Patient selection for device-based antihypertensive therapy:

- When selecting the best device-based hypertension therapy for each particular patient, the procedural risk must not be greater than the danger associated with the underlying illness directly. [20]
- Patients with hypertension that is difficult to control may benefit the most from device-based hypertension therapy in normal clinical care. Patients need to be informed in a balanced manner regarding the blood pressure response's variability, the consequences of blood pressure lowering's unknowable side effects, and long-term safety. [21]
- The most suitable group for future clinical studies in the use of devices to treat hypertension should be high-risk hypertensive patients with comorbidities such CAD, diabetes, and CKD in the short term (2–3 years). [22]
- Future research should examine shifting the emphasis from treating severe and resistant hypertension to including individuals who have mild to moderately increased blood pressure. [23][24]

Hypertension Medication Adherence:

One of the main causes of poor blood pressure regulation is thought to be medication non-adherence. The medicine schedule typically calls for more than three pill doses, which makes it difficult for the patient to follow it. [25] Patients who use one stick with the treatment more consistently. They can easily remember the medication and properly give it because of this.

People who faithfully followed the medication regimen were found to have greater control over their hypertension and make up more than 45% of the population. [26].

Lack of adherence of hypertension can be accounted for the following reasons:

1. **Prescription error:**

The prescribing error is a common drug error that can be prevented in hospitals around the world. The study found that up to 6.2% of drugs ordered during hospital stays in the USA and the UK had mistakes. [27]. It was shown that 70% of drug errors were due to prescription errors. [28]. According to the study, medication errors (MEs) were to blame for one-third of adverse drug reactions (ADR) in Saudi Arabia. [29]. According to the National Coordinating Council for Medicine Error Reporting and Prevention, handwriting issues, abbreviation issues, and incomplete pharmaceutical orders account for 15% of medication errors. [30] A minimum of one inaccuracy per prescription was recorded in the study conducted in Eastern Nepal. [31]. A study of elderly patients at a Nepalese teaching hospital found that there were potentially more mistakes with prescriptions. They discovered that 53% of patients had at least one potentially inappropriate prescription supplied to them, and that each patient had an average of 0.37 drug interactions. [32] [33].

2. **Forgetfulness:**

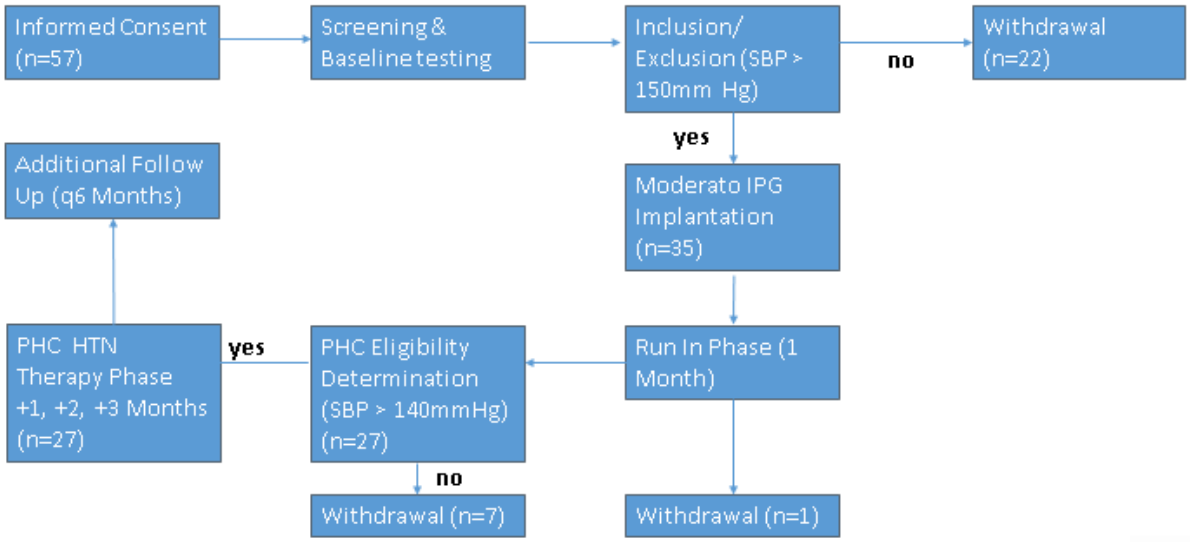
It may be difficult at first to incorporate taking medication into your daily routine, just like it is to form any new habit. To remain consistent, you need motivation, accountability, and prompts. Even seasoned mediators occasionally skip dosages because of scheduling conflicts or environment changes. People often neglect ordinary tasks, even when they are important. When taking medication, reminders are necessary because it's likely that a new drug will impair your memory. [34] [35]

3. **Complex medication schedule:**

With complex medication regimens, you need to assist your medication organisation in addition to setting reminders for when to take dosages throughout the day. Some patients, such as children, could need help from others to take their medications. Having a companion or caretaker on board is advantageous because accountability aids a patient in staying on track. Reminders that a medication has run out can be added to help patients be more proactive and maintain their adherence. [36] [37]

Programmable Hypertension Control [PHC] Therapy:

Comparing PHC therapy to traditional device-based therapies for hypertension can reveal a variety of possible advantages. The capacity to "tune" and alter PHC therapy as required to achieve personalized blood pressure control is the first. The ability to quickly detect acute blood pressure reactions, particularly the presence or absence of a blood pressure overshoot when PHC pacing is stopped, is a useful tool for adjusting the degree of blood pressure reduction and evaluating the impact on sympathetic activation (at least in the acute setting). In contrast, with other therapies, the treatment is "all or none" and the outcomes aren't usually obvious right away. Second, since the technique modifies both ventricular filling and baroreflexes, it is possible that PHC therapy mimics the effects of a number of different drug classes and can be utilised to treat individuals with isolated systolic hypertension. A concern with extended right ventricular pacing could be heart failure. When a pacemaker with considerable right ventricular pacing was later implanted in people with normal or low LVEF, up to 26% of those people developed clinical heart failure symptoms.



Study Procedure:

- The patients gave their informed consent. Patients whose use of a dual chamber pacemaker is advised were included in the study.
- A two-day eligibility test was held (one week apart from each day). Patients were deemed possibly eligible if their average systolic pressure was less than 150mmHg and their systolic pressure on average was greater than 140mmHg on both tests. Additionally, the patients received echocardiography, 24-hour ambulatory systolic blood pressure (24hABSP) monitoring, and a blood test to check the renal function.
- Without the PHC algorithm activation, the patients had the Moderato IPG implanted. Patients who met the inclusion criteria for at least two to four weeks were included in the RUN-IN Phase of the study, which was followed by a three-month study. The PHC began to function at this point, and the beginning of the study (time=0) was determined by the PHC's activation at that point.
- The PHC algorithm was activated over the following three months for the primary safety and efficacy evaluation on patients who met the eligibility requirements after the RUN-IN Phase. The blood pressure was recorded using a non-invasive technique as part of the PHC algorithm's optimization. PHC activation was monitored and documented. By changing the PHC treatment settings, in particular the values for the shorter and longer atrioventricular intervals and the number of beats with each atrioventricular interval, a significant and consistent drop in SBP of at least 5 mm Hg was achieved.
- For 1, 2, and 3 months, PHC therapy was recommended to the patients. Each appointment included a blood test, heart echocardiography, and a blood pressure measurement with and without PHC.
- Blood tests were added during the visits in the second month of the experiment, and ambulatory blood pressure monitoring was implemented halfway through the first month. A six-month break was added to the PHC therapy at the end of the third month so that the safety and device functionality could be evaluated. For the following two years, blood tests and blood pressure readings were performed.
- An impartial Data Safety Monitoring Board was in charge of keeping an eye on the trial; it made decisions on all major adverse occurrences and examined overall safety information.

Limitations:

The nonrandomized trial design, the small number of patients involved, and the relatively brief follow-up time are the key drawbacks of the current first-in-human study. Strong effectiveness indications and a high safety record from the current trial demand further research into strategies for overcoming these restrictions.

Furthermore, although it has not been studied, PHC pacing's possible effects on exercise tolerance should be taken into account in future research.

Conclusions:

Using a pacemaker-based device to pace the heart with varyingly timed shorter and longer atrioventricular intervals to treat hypertension is safe and effective, according to preliminary data from this first-in-human research. The risks associated with pacemaker insertion or replacement would have applied to the patients regardless of whether they took part in the trial or used PHC pacing therapy. As a result, the study greatly improves the therapy's safety profile. Another benefit of PHC therapy over other device-based therapies is the ability to "tune" it was necessary to offer individualised blood pressure control. According to the study conducted thus far, this therapy lowers blood pressure temporarily without displaying any signs of sympathetic activation. More information is required to evaluate safety (Effects on LV size and function, atrial size, and arrhythmias), as well as the impact on sympathetic nerve activity and efficacy, in longer-term randomised studies. Greater evidence of its effectiveness and safety could lead to the availability of such a therapy for those who do not require pacemakers.

Reference:

1. Kuroda, Kagayaki, and Satoshi Yatsushiro. "New insights into MR safety for implantable medical devices." *Magnetic Resonance in Medical Sciences* 21, no. 1 (2022): 110-131..
2. Zito, Andrea, Giuseppe Princi, Marco Lombardi, Domenico D'Amario, Rocco Vergallo, Cristina Aurigemma, Enrico Romagnoli et al. "Long-term clinical impact of permanent pacemaker implantation in patients undergoing transcatheter aortic valve implantation: a systematic review and meta-analysis." *EP Europace* (2022).
3. Gonzalez-Melchor, L., J. L. Martinez-Sande, J. Garcia-Seara, M. Rodriguez-Manero, X. A. Fernandez-Lopez, C. Minguito-Carazo, T. Gonzalez, and J. R. Gonzalez Juanatey. "Conventional single-chamber pacemakers versus transcatheter pacing systems at long-term follow-up." *European Heart Journal* 43, no. Supplement_2 (2022): ehac544-714..
4. Alexander, Nebu, Apostolos Tsimploulis, Arooge Towheed, Cyrus Adel Hadadi, Zayd A. Eldadah, and Seth J. Worley. "PO-686-03 BIVENTRICULAR PACEMAKER IMPLANTATION IN A PATIENT WITH CONGENITALLY OCCLUDED SVC." *Heart Rhythm* 19, no. 5 (2022): S380-S381.
5. Kaza, N., V. Htun, A. Miyazawa, F. Simader, B. Porter, J. P. Howard, A. Arnold et al. "A systematic review and meta-analysis of upgrade to biventricular or conduction system pacing approaches." *European Heart Journal* 43, no. Supplement_2 (2022): ehac544-736.
6. Gill, Jashan. "Emerging Technologies in Electrophysiology: From Single-Chamber to Biventricular Leadless Pacemakers." *Cardiology* 147, no. 2 (2022): 179-190.
7. Baik, Jinhwan, Hwanik Kim, Sangyong Lee, Dae Hyoung Park, Minh-Tung Do, Hae-Yong Lee, Eue-Keun Choi, Sunchoel Yang, Chang Wook Jeong, and Sung-min Park. "Laparoscopic ablation system for complete circumferential renal sympathetic denervation." *IEEE Transactions on Biomedical Engineering* 68, no. 11 (2021): 3217-3227.
8. Fengler, Karl. "Renal Denervation for Resistant Hypertension: A Concise Update on Treatment Options and the Latest Clinical Evidence." *Cardiology and Therapy* (2022): 1-8.
9. Agasthi, Pradyumna, Justin Shipman, Reza Arsanjani, Moses Ashukem, Marlene Girardo, Charan Yerasi, Nithin Venepally, Floyd David Fortuin, and Farouk Mookadam. "Renal denervation for resistant hypertension in the contemporary era: a systematic review and meta-analysis." *Scientific reports* 9, no. 1 (2019): 1-9.
10. Mahfoud, Felix, Markus Schlaich, Michael Boehm, Murray Esler, and Thomas Felix Luescher. "Catheter-based renal denervation: the next chapter begins." *European Heart Journal* 39, no. 47 (2018): 4144-4149.
11. Lobo, Melvin D., Andrew SP Sharp, Vikas Kapil, Justin Davies, Mark A. de Belder, Trevor Cleveland, Clare Bent et al. "Joint UK societies' 2019 consensus statement on renal denervation." *Heart* 105, no. 19 (2019): 1456-1463.
12. Guzik, Mateusz, Szymon Urban, Gracjan Iwanek, Jan Biegus, Piotr Ponikowski, and Robert Zymliński. "Novel therapeutic devices in heart failure." *Journal of Clinical Medicine* 11, no. 15 (2022): 4303.
13. Groenland, Eline H., and Wilko Spiering. "Baroreflex amplification and carotid body modulation for the treatment of resistant hypertension." *Current hypertension reports* 22, no. 4 (2020): 1-8.

14. Camafort M, Chung WJ, Shin JH. Role of ambulatory blood pressure monitoring in elderly hypertensive patients. Clinical hypertension. 2022 Dec;28(1):1-6.

15. Pisano, Anna, Francesca Mallamaci, Graziella D'arrigo, Davide Bolignano, Gregoire Wuerzner, Alberto Ortiz, Michel Burnier et al. "Assessment of hypertension in kidney transplantation by ambulatory blood pressure monitoring: a systematic review and meta-analysis." *Clinical kidney journal* 15, no. 1 (2022): 31-42.
16. Guckel, Denise, Thomas Eitz, Mustapha El Hamriti, Martin Braun, Moneeb Khalaph, Guram Imnadze, Thomas Fink et al. "Baroreflex activation therapy in advanced heart failure therapy: insights from a real-world scenario." *ESC Heart Failure* (2022).

17. Clemmer, John S., and W. Andrew Pruett. "Modeling the physiological roles of the heart and kidney in heart failure with preserved ejection fraction during baroreflex activation therapy." *American Journal of Physiology-Heart and Circulatory Physiology* 323, no. 3 (2022): H597-H607.
18. van Kleef, Monique EAM, Chandan M. Devireddy, Jan van der Heyden, Mark C. Bates, George L. Bakris, Gregg W. Stone, Bryan Williams, Wilko Spiering, and CALM-FIM Investigators. "Treatment of resistant hypertension with endovascular baroreflex amplification: 3-year results from the CALM-FIM study." *Cardiovascular Interventions* 15, no. 3 (2022): 321-332.
19. Piayda, Kerstin, Kolja Sievert, Horst Sievert, Tamaz Shaburishvili, Irakli Gogorishvili, Martin Rothman, James L. Januzzi Jr, JoAnn Lindenfeld, and Gregg W. Stone. "Endovascular Baroreflex Amplification With the MobiusHD Device in Patients With Heart Failure and Reduced Ejection Fraction: Interim Analysis of the First-in-Human Results." *Structural Heart* 6, no. 5 (2022): 100086.
20. Jami, Oussama, Youssef Tijani, and Aziz Et-Tahir. "Device-Based Therapy for Resistant Hypertension: An Up- to- Date Review." *High Blood Pressure & Cardiovascular Prevention* (2022): 1-10.
21. Ojji, Dike B., Victoria Cornelius, Giles Partington, Veronica Francis, Shahiemah Pandie, Wynand Smythe, Nicky Hickman et al. "Effect of 3, 2-Drug Combinations of Antihypertensive Therapies on Blood Pressure Variability in Black African Patients: Secondary Analyses of the CREOLE Trial." *Hypertension* (2022): 10-1161.
22. Mulatero, Paolo, Chiara Bertello, Franco Veglio, and Silvia Monticone. "Approach to the Patient on Antihypertensive Therapy: Screen for Primary Aldosteronism." *The Journal of Clinical Endocrinology & Metabolism* (2022).
23. Tadic, Marijana, Elisa Gherbesi, Carla Sala, Stefano Carugo, and Cesare Cuspidi. "Effect of long-term antihypertensive therapy on myocardial strain: a meta-analysis." *Journal of Hypertension* 40, no. 4 (2022): 641-647.
24. Xie, Lin, Feride Frech-Tamas, Elizabeth Marrett, and Onur Baser. "A medication adherence and persistence comparison of hypertensive patients treated with single-, double-and triple-pill combination therapy." *Current Medical Research and Opinion* 30, no. 12 (2014): 2415-2422.
25. Bramley, Thomas J., Brian S. Nightengale, Feride Frech-Tamas, and Phillip P. Gerbino. "Relationship of blood pressure control to adherence with antihypertensive monotherapy in 13 managed care organizations." *Journal of Managed Care Pharmacy* 12, no. 3 (2006): 239-245.
26. Tully, Mary P., and Iain E. Buchan. "Prescribing errors during hospital inpatient care: factors influencing identification by pharmacists." *Pharmacy world & science* 31, no. 6 (2009): 682-688..
27. Velo, Giampaolo P., and Pietro Minuz. "Medication errors: prescribing faults and prescription errors." *British journal of clinical pharmacology* 67, no. 6 (2009): 624-628.
28. Ali, Sheraz, Nourah Ibrahim Aboheimed, Ibrahim Abdulaziz Al-Zaagi, and Dalal Salem Al-Dossari. "Analysis of medication errors at a large tertiary care hospital in Saudi Arabia: a retrospective analysis." *International journal of clinical pharmacy* 39, no. 5 (2017): 1004-1007.
29. Ather, A., P. Neelkantreddy, G. Anand, G. Manjunath, J. Vishwanath, and M. Riyaz. "A study on determination of prescription writing errors in outpatient department of medicine in a teaching Hospital." *Indian Journal of Pharmacy Practice* 6, no. 2 (2013).
30. Joshi, Anuradha, Jatin Buch, Nitin Kothari, and Nishal Shah. "Evaluation of hand written and computerized out-patient prescriptions in urban part of Central Gujarat." *Journal of Clinical and Diagnostic Research: JCDR* 10, no. 6 (2016): FC01.
31. Sapkota, Sujata, Nawin Pudasaini, Chandan Singh, and G. C. Sagar. "Drug prescribing pattern and prescription error in elderly: A retrospective study of inpatient record." *Asian j pharm clin res* 4, no. 3 (2011): 129-32..

32. Roumeliotis, Nadia, Jonathan Sniderman, Thomasin Adams-Webber, Newton Addo, Vijay Anand, Paula Rochon, Anna Taddio, and Christopher Parshuram. "Effect of electronic prescribing strategies on medication error and harm in hospital: a systematic review and meta-analysis." *Journal of general internal medicine* 34, no. 10 (2019): 2210-2223.
33. Nieuwlaat, Robby, Nancy Wilczynski, Tamara Navarro, Nicholas Hobson, Rebecca Jeffery, Arun Keepanasseril, Thomas Agoritsas et al. "Interventions for enhancing medication adherence." *Cochrane database of systematic reviews* 11 (2014).
34. Vervloet, Marcia, Annemiek J. Linn, Julia CM van Weert, Dinny H. De Bakker, Marcel L. Bouvy, and Liset Van Dijk. "The effectiveness of interventions using electronic reminders to improve adherence to chronic medication: a systematic review of the literature." *Journal of the American Medical Informatics Association* 19, no. 5 (2012): 696-704.
35. DePhillips, Catherine, Puja B. Parikh, and Gregg A. Stevens. "Dyslipidemia: Current Therapies and Strategies to Overcome Barriers for Use." *The Journal for Nurse Practitioners* 17, no. 10 (2021): 1167-1173.
36. Shrestha, Shakti, Roshan Giri, Hari Prasad Sapkota, Siddhartha Sharma Danai, Ahsan Saleem, Shreeshab Devkota, Sagar Shrestha, Bhojraj Adhikari, and Arjun Poudel. "Attitudes of ambulatory care older Nepalese patients towards deprescribing and predictors of their willingness to deprescribe." *Therapeutic advances in drug safety* 12 (2021): 20420986211019309.
37. Brignole, Michele, and Richard Sutton. "Left bundle branch area pacing in perspective." *European Heart Journal* (2022).
38. Miyoshi, Fumito, Youichi Kobayashi, Hiroyuki Itou, Tatsuya Onuki, Takaaki Matsuyama, Norikazu Watanabe, Chungchang Liu et al. "Prolonged paced QRS duration as a predictor for congestive heart failure in patients with right ventricular apical pacing." *Pacing and clinical electrophysiology* 28, no. 11 (2005): 1182-1188.
39. ZHANG, XUE- HUA, H. U. A. Chen, CHUNG- WAH SIU, KAI- HANG YIU, WING- SZE CHAN, Kathy L. Lee, HON- WAH CHAN et al. "New- onset heart failure after permanent right ventricular apical pacing in patients with acquired high- grade atrioventricular block and normal left ventricular function." *Journal of cardiovascular electrophysiology* 19, no. 2 (2008): 136-141.