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STATE OF THE ART

Cardiac Memory – from Theory to Clinical Practice

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ABSTRACT

Cardiac memory (CM) is defined as changes in T wave polarity and vector that appear after cessation of a period of abnormal ventricular depolarization of various causes.

The mechanisms responsible for CM development are initiation by local stretch, requiring myocardial contraction, followed by a cascade of intracellular signals that lead to a reduction in repolarization currents, especially I_{to}.

In practice, CM is a frequently encountered ECG phenomenon, especially in patients with intermittent ventricular pacing, and knowledge of the ECG pattern of CM may help quick differential diagnosis from ischemia. While CM is most often a benign finding, in rare cases, association between CM and severe bradycardia or other factors for QT prolongation may be pro-arrhythmic and requires emergency care.

Keywords: cardiac memory, T wave.

DEFINITION

Cardiac memory (CM) is defined as repolarization changes secondary to a transient period of abnormal ventricular activation. After this abnormal activation ceases, the repolarization (T wave) vector aligns with the vector of the "abnormally" activated QRS complex.

I. Theoretical aspects

The term "cardiac memory" and its main attributes have been formulated by Mauricio Rosenbaum in 1982 (1). Briefly, Rosenbaum characterized CM by the following: the T wave vector in sinus rhythm aligns with the vector of the previous "abnormal" QRS complex; the amplitude of the memory T wave increases with increased duration of the prior abnormal activation; and after normalization of the T wave, repeated episodes of abnormal activation result in a faster and more marked appearance of CM changes.

Mechanisms and classification

While the molecular mechanisms underlying CM are not entirely uncovered, many studies on animal models have found key links in its development.

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In short, CM genesis appears to be unrelated to local ischemia or structural changes (2). Induction of CM is dependent (2, 3) on local stretch, which activates stretch receptors regionally and increases local levels of angiotensin II. Decoupling excitation from contraction seems to abolish development of CM (3), accentuating the idea that CM is dependent on myocardial contractility, and not simply an electrical phenomenon. The association of post-pacing CM with regional dispersion of action potential duration and local strain in canine models (2) may suggest pro-arrhythmic capacity.

The underlying molecular mechanisms for appearance of CM changes are reduction in repolarization currents ($I_{to,}$), particularly I_{to} (4, 5), with loss of the action potential notch and prolongation of action potential duration in epicardial cells (4). This is mediated by angiotensin II and the microtubule network [6], and also by the $I_{Ca,L}$ current and increased intracellular calcium concentration (7, 8), leading to changes in nuclear transcription factors. Further proof of the key role of I_{to} in CM induction was derived from a study that confirmed that CM changes did not appear in hearts of neo-natal dogs, which do not yet express I_{to} (9).

It should be noted that, without detracting from the importance of studies at cellular level, the observations derived from them cannot be directly applied in clinical situations. For example, a study on human subjects with permanent cardiac pacing failed to show an influence of angiotensin receptor blockers (losartan) or calcium-channel blockers (diltiazem) on electrical memory changes (10).

Cardiac memory has been classified into two forms (11): (i) short-term CM (induced by less than two hours of ventricular pacing; these CM changes have a duration of minutes to hours) and (ii) long-term CM (induced by 2-3 weeks of ventricular pacing; these CM changes have a duration of weeks to months). Most clinical aspects and studies of CM in human subjects generally relate to long-term changes.

II. Clinical focus

In clinical practice, CM is encountered as T wave changes following periods of altered ventricular activation, such as intermittent bundle branch block (BBB) (12), ventricular preexcitation (13), ventricular pacing (1, 14), frequent premature ventricular contractions (15) or ventricular tachycardia (16), and even after QRS widening following antiarrhythmic drug toxicity (17).

ECG description

For the clinician, CM appears as T wave inversions in the leads where the previously "abnormal" QRS complex was negative, and positive T waves in the leads where the previously "abnormal" QRS complex was positive.

These changes can only be observed if the abnormal ventricular activation is intermittent, so as to allow periods of normal (or same as baseline) activation over the His-Purkinje system and thus unmask CM. In a patient with permanent ventricular pacing, it is therefore necessary to have periods of paced rhythm and periods of spontaneous conduction (Figure 1), and in a pa-

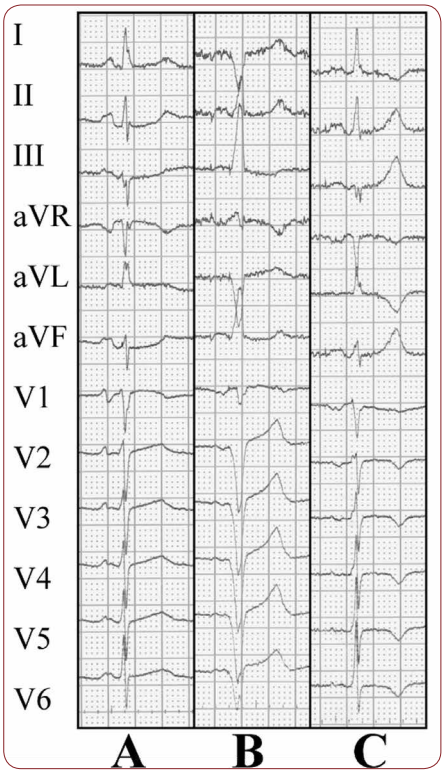

FIGURE 1. ECG example (paper speed 25 mm/s, scale 10 mm/mV) of post-pacing cardiac memory in a patient with DDD pacemaker and septal position of the right ventricular lead. Panel A: baseline ECG, panel B: ventricular pacing with short atrio-ventricular interval, panel C: post-pacing cardiac memory, seen as negative T waves in the leads where the paced QRS complex was negative and positive T waves in the leads where the paced QRS complex was positive.

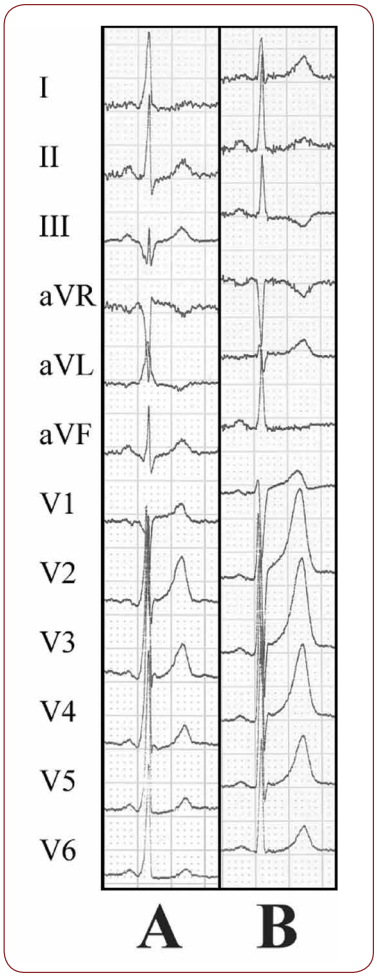

FIGURE 2. ECG example (paper speed 25 mm/s, scale 10 mm/mV) of cardiac memory in a patient with ventricular pre-excitation. Panel A: initial ECG, showing ventricular pre-excitation over a postero-septal accessory pathway, with negative delta waves in the inferior leads. Panel B: ECG after radiofrequency ablation of accessory pathway, showing ventricular activation entirely over the His-Purkinje system (normal PR interval, narrow QRS, disappearance of delta waves) and cardiac memory, seen as negative T waves in the leads where the delta wave was negative, and tall positive T waves in the leads where the delta wave was positive.

tient with ventricular pre-excitation CM may be seen if the pre-excitation is intermittent, but more often after ablation of the accessory pathway (Figure 2).

Differential diagnosis between CM and ischemia

Discrimination from ischemia is a key clinical aspect, as negative T waves can be seen in both conditions, and ECG criteria have been proposed for differentiation of ischemia from CM post-idiopathic left ventricular tachycardia (16) and from CM post-apical pacing (18).

This differential diagnosis is especially important for post-pacing CM, as it is frequently encountered in the same age group where myocardial ischemia is common. In a study published in 2005 (18), the authors found surface ECG criteria that discriminated CM post-pacing from the right ventricular apex from ischemia. Thus, the combination of (1) positive T in aVL (2) positive or isoelectric T in lead I, and (3) maximal precordial TWI>TWI in lead III was found to have a sensitivity of 92% and a specificity of 100% for CM.

One simple rule in clinical practice in an asymptomatic patient would be to ascertain whether the pattern of negative and positive T waves in each lead respects the rules of cardiac memory when compared to an ECG with paced QRS complexes. If so, then cardiac memory is the likely cause for the repolarization changes, and this may help avoiding unnecessary testing in asymptomatic subjects. If abnormal negative T waves appear in leads where the paced QRS complex was positive, or if the patient has symptoms of ischemia, the latter is the probable cause of the repolarization changes and further assessment and treatment are needed, according to current guidelines (19). We note there have been no studies to date concerning differentiation between ischemia and post-pacing CM from alternate (non-apical) right ventricular pacing sites, nor concerning aspects of post-pacing CM in patients with associated myocardial ischemia or hypertrophy.

Cardiac memory in wide QRS rhythms

Cardiac memory has usually been described in narrow QRS rhythms (sinus rhythm with normal His-Purkinje conduction). However, the same principle of "memory" T waves remains valid if the baseline rhythm has a wide QRS. Such CM changes are rarer in the clinical setting, and more care is needed when interpreting them in individual patients.

T wave changes typical of CM have been described in patients with heart failure, baseline left BBB and CRT devices. Bi-ventricular pacing was followed by CM superimposed on the secondary T wave changes of the existing left BBB (20, 21).

Reports of CM in cases with intermittent multiple infra-hisian conduction anomalies have also

been described, such as CM changes in patients with alternating tri-fascicular block (22).

Can CM be dangerous (pro-arrhythmic)?

In most cases, CM changes are considered benign and have not been generally associated with an increased risk of ventricular arrhythmias in patients with normal conduction; in most studies, the QTc interval was normal or only mildly prolonged in CM patients (16, 18).

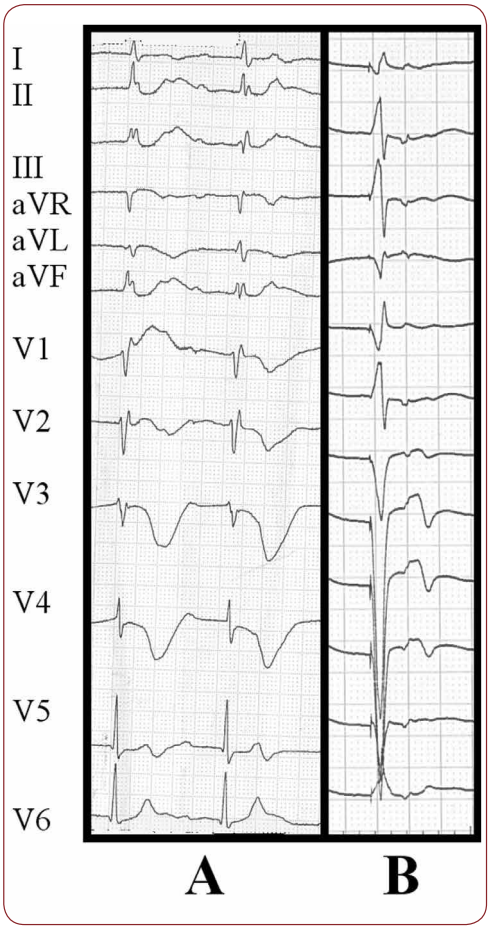

FIGURE 2. ECG example (paper speed 25 mm/s, scale 10 mm/mV) of possible implication of cardiac memory in arrhythmogenesis. Panel A shows an idioventricular rhythm at 55/min in a patient with single-chamber VVI(R) pacemaker, programmed with hysteresis at 40/min. Panel B shows paced rhythm in the same patient at VVI 75/min after 24 hours. Note that the idioventricular rhythm has a QRS vector markedly different from that of the paced QRS, and that the pattern of negative T waves in this rhythm respects the "rules" of post-pacing cardiac memory. The QTc interval is very prolonged (663 ms) during ventricular rhythm, and cardiac memory may contribute to these potentially arrhythmogenic changes.

However, association of pro-arrhythmic factors in addition to CM may be problematic. There has been one reported case (23) of polymorphic ventricular tachycardia associated partly with cardiac memory after accessory pathway ablation, however in that case prolonged QT interval was also observed, caused by other factors (treatment with Sotalol). Another case (24) implicating CM in the induction of long QT and torsades de pointes related to a pacemaker patient who developed an atypical junctional rhythm associated with hypokalemia while attempting to avoid ventricular pacing by lowering the pacing rate. A similar example from our practice is shown in Figure 3, in a case of low-rate hysteresis pacemaker setting in a patient with no other factors for QT prolongation.

The risk of torsades de pointes during atrioventricular (AV) block, in patients with a known prior ECG has been associated with the magnitude of change in QRS morphology and axis during AV block, suggesting that CM may be a factor in QT prolongation and ventricular arrhythmia during high-grade AV block (25).

To summarize, CM changes may have arrhythmogenic potential in the setting of severe bradycardia or high-grade AV conduction anomalies, or if associated with other causes for significant QT prolongation, probably due to the alterations in gradients of repolarization currents that underlie CM development.

CONCLUSIONS

Cardiac memory is a frequently encountered ECG phenomenon, especially in patients with ventricular pacing, and is most often a benign finding. Knowledge of the ECG pattern of CM may help quick differential diagnosis from ischemia for the clinician. Rarely, association between CM and severe bradycardia or other factors for QT prolongation may be pro-arrhythmic and require emergency care. Further studies are needed to assess CM changes in more complex patients, especially those with multiple causes for repolarization abnormalities, and also to better define potential "at risk" cases. ❑

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References

1. **Rosenbaum MB, Blanco HH, Elizari MV, et al.** Electrotonic modulation of the T wave and cardiac memory. *Am J Cardiol* 1982;50:213-222.
2. **Jeyaraj D, Wilson LD, Zhong J, et al.** Mechanoelectrical feedback as novel mechanism of cardiac electrical remodeling. *Circulation* 2007;115:3145-3155.
3. **Sosunov EA, Anyukhovsky EP, Rosen MR.** Altered ventricular stretch contributes to initiation of cardiac memory. *Heart Rhythm* 2008;5:106-113.
4. **Yu H, McKinnon D, Dixon JE, et al.** Transient outward current, Ito1, is altered in cardiac memory. *Circulation* 1999;99:1898-1905.
5. **Geller JC, Rosen MR.** Persistent T-wave changes after alteration of the ventricular activation sequence. New insights into cellular mechanisms of 'cardiac memory'. *Circulation* 1993;88:1811-1819.
6. **Özgen N, Lu Z, Boink GJ, et al.** Microtubules and angiotensin II receptors contribute to modulation of repolarization induced by ventricular pacing. *Heart Rhythm* 2012;9:1865-1872.
7. **Plotnikov AN, Yu H, Geller JC, et al.** Role of L-type calcium channels in pacing-induced short-term and long-term cardiac memory in canine heart. *Circulation* 2003;107:2844-2849.
8. **Patberg KW, Plotnikov AN, Quamina A, et al.** Cardiac memory is associated with decreased levels of the transcriptional factor CREB modulated by angiotensin II and calcium. *Circ Res* 2003;93:472-478.
9. **Plotnikov AN, Sosunov EA, Patberg KW, et al.** Cardiac memory evolves with age in association with development of the transient outward current. *Circulation* 2004;110:489-495.
10. **Chiale PA, Etcheverry D, Pastori JD, et al.** Clinical evaluation of losartan and diltiazem on the development of T-wave memory by right apical ventricular pacing. *J Am Coll Cardiol* 2014;63:1929-1931.
11. **Ozgen N, Rosen MR.** Cardiac memory: a work in progress. *Heart Rhythm* 2009;6:564-570.
12. **Denes P, Pick A, Miller RH, et al.** A characteristic precordial repolarization abnormality with intermittent left bundle-branch block. *Ann Intern Med* 1978;89:55-57.
13. **Kalbfleisch SJ, Sousa J, el-Atassi R, et al.** Repolarization abnormalities after catheter ablation of accessory atrioventricular connections with radiofrequency current. *J Am Coll Cardiol* 1991;18:1761-1766.
14. **Waks JW, Steinhaus DA, Shvilkin A, et al.** Post-pacemaker T-wave Inversions: Cardiac Memory. *Am J Med* 2016;129:170-172.
15. **Sakamoto Y, Inden Y, Okamoto H, et al.** T-wave changes of cardiac memory caused by frequent premature ventricular contractions originating from the right ventricular outflow tract. *J Cardiovasc Electrophysiol* 2019 Jun 3. Advance online publication.
16. **Nakagawa T, Yagi T, Ishida A, et al.** Differences between cardiac memory T wave changes after idiopathic left ventricular tachycardia and ischemic T wave inversion induced by acute coronary syndrome. *J Electrocardiol* 2016;49:596-602.
17. **Wylie JV Jr, Zimetbaum P, Josephson ME, et al.** Cardiac memory induced by QRS widening due to propafenone toxicity. *Pacing Clin Electrophysiol* 2007;30:1161-1164.
18. **Shvilkin A, Ho KK, Rosen MR, et al.** T-vector direction differentiates postpacing from ischemic T-wave inversion in precordial leads. *Circulation* 2005;111:969-974.
19. **Brignole M, Auricchio A, Baron-Esquivias G, et al.** 2013 ESC guidelines on cardiac pacing and cardiac resynchronization therapy: the task force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA). *Europace* 2013;15:1070-1118.
20. **Wecke L, van Deursen CJ, Bergfeldt L, et al.** Repolarization changes in patients with heart failure receiving cardiac resynchronization therapy-signs of cardiac memory. *J Electrocardiol* 2011;44:590-598.
21. **Padeletti L, Fantappiè C, Perrotta L, et al.** Cardiac memory in humans: vectocardiographic quantification in cardiac resynchronization therapy. *Clin Res Cardiol* 2011;100:51–56.
22. **Danon A, Shurrab M.** Alternating trifascicular block and cardiac memory. *J Electrocardiol* 2017;50:966-968.
23. **Haverkamp W, Hördt M, Breithardt G, et al.** Torsade de pointes secondary to d, l-sotalol after catheter ablation of incessant atrioventricular reentrant tachycardia – evidence for a significant contribution of the "cardiac memory". *Clin Cardiol* 1998;21:55-58.
24. **Kurita T, Ohe T, Maeda K, et al.** QRS alteration-induced torsade de pointes in a patient with an artificial pacemaker and hypokalemia. *Jpn Circ J* 1996;60:189-191.
25. **Rosso R, Adler A, Strasberg B, et al.** Long QT syndrome complicating atrioventricular block: arrhythmogenic effects of cardiac memory. *Circ Arrhythm Electrophysiol* 2014;7:1129-1135.