**Supplemental file**

**Clinical and genetic characteristics of catecholaminergic polymorphic ventricular tachycardia combined with left ventricular non-compaction**

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***Variant determination***

Genomic DNA was extracted from peripheral blood leukocytes. All coding exons and flanking regions of candidate genes were enriched using a custom-designed library (Agilent Technologies, Santa Clara, CA, USA), and subsequently sequenced on a Genome Analyzer Hiseq 2500 system (Illumina Inc., CA, USA). Sequencing reads were mapped to the human reference genome (GRCh37/hg19) with BWA (Version: 0.7.12-r1039). After the removal of PCR duplications with PICARD (Version: 1.112), variants were called using Varscan (Version: 2.2.5).

Rare variants were defined according to the minor allele frequency <0.00005 in the 1,000 Genomes Project, ExAC Exome Aggregation Consortium, Exome Variant Server, NHLBI GO Exome Sequencing Project (ESP), Seattle, WA (URL: http://evs.gs.washington.edu/EVS); and were classified using the 2015 American College of Medical Genetics and Genomics guidelines to allow for the contemporary assessment of prevalence and characterization as “pathogenic,” “likely pathogenic,” “benign,” “likely benign,” or “variant of unknown significance (VUS).”

***The list of targeted genes：***

*ABCB1, ABCC9, AKAP9, ALG10, ANK2, BAG3, CACNA1C, CACNA2D1, CACNB2, CALM1, CALM2, CALM3, CASQ2, CAV3, CAVIN1, CDH2, CELF4, CERKL, CTNNA3, CYP2B6, CYP2C19, CYP2C9, CYP2D6, DBH, DES, DNAJC19, DPP6, DSC2, DSG2, DSP, FLNC, GATA5, GATA6, GJA1, GJA5, GNAI2, GPD1L, HADHA, HCN4, JUP, KCNA5, KCND2, KCND3, KCNE1, KCNE2, KCNE3, KCNE5, KCNH2, KCNJ2, KCNJ5, KCNJ8, KCNQ1, LDB3, LMNA, MYH6, MYH7, MYL4, NKX2-5, NOS1AP, NPPA, NRG3, NUBPL, NUP155, PKP2, PLN, PPA2, PRKAG2, RYR2, SALL4, SCN10A, SCN1B, SCN2B, SCN3B, SCN4B, SCN5A, SDHAF3, SLC22A23, SLCO3A1, SNTA1, TBX5, TECRL, TGFB3, TMEM43, TNNI3, TNNI3K, TNNT2, TRDN, TRPM4, TTN* ；

***Summarization of clinical and genetic information of 24 CPVT patients***

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Case** | **Sex** | **Age at onset**  **(year)** | **Age at diagnosis**  **(year)** | **Phenotype** | **Most severe episodes** | **QTc (ms)** | **Most severe arrhythmia during EST or Holter** | **Echocardiography** | | **Gene sequencing** | | | **Medication**  **dose/day** | **ICD/PM/LCSD/RFCA** | **Follow-up period**  **(years)** |
| **NC/C** | **EF%** | **Method** | **Variant** | **Acid change** |
| 1 | F | 9 | 12 | CPVT-LVNC | Syncope | 426 | bVT/pVT | 2.3 | 73 | WES | RyR2-  c.5278C＞T | R1760W | Metoprolol  71.25mg  Flecainide  100mg | PM | SCD  Aged 14 during playing |
| 2 | M | 5 | 6 | CPVT-LVNC | Syncope | 458 | bVT/pVT | 1.6 | 70 | WES | RyR2-  c.12014A＞T | E4005V | Metoprolol  118.75mg | - | SCD  Aged 8 during skiing |
| 3  Mother of case 2 | F | 12 | 35 | CPVT-LVNC | Syncope | 392 | bVT/pVT | 2.2 | 60 | Familial verification | RyR2-  c.12014A＞T | E4005V | Metoprolol  47.5mg | LCSD | 5 |
| 4 | F | 1 | 27 | CPVT-LVNC | Syncope | 374 | bVT | 2.3 | 56 | WES | CASQ2- c.196A＞G | T66A | Propranolol  15mg | - | 1 |
| 5 | F | 15 | 16 | CPVT-LVNC | CPA | 423 | pVT | 2 | 67 | No | - | - | Verapamil  90mg | - | 15 |
| 6 | M | 11 | 14 | CPVT | Syncope | 419 | bVT/pVT | - | 60 | WES | RyR2-  c.1298T＞C | L433P | Propranolol  60mg | - | 10 |
| 7  Sister of case 6 | F | 21 | 35 | CPVT | Syncope | 403 | bVT/pVT | - | 73 | Familial verification | RyR2-  c.1298T＞C | L433P | No medication | - | 10 |
| 8  Son of case 7 | M | 11 | 11 | CPVT | None | 409 | None | - | 65 | Familial verification | RyR2-  c.1298T＞C | L433P | No medication | - | 10 |
| 9 | F | 9 | 10 | CPVT | Syncope | 395 | PVC bigeminy | - | 67 | WES | RyR2- c.6949G＞A | A2317T | Metoprolol  118.75mg | - | 8 |
| 10 | M | 8 | 8 | CPVT | Syncope | 379 | bVT/pVT | - | 69 | WES | RyR2-  c.11836G＞A | G3946S | Metoprolol  75mg | - | 4 |
| 11  Mother of case 10 | F | 32 | 42 | CPVT | Syncope | 409 | PVC bigeminy | - | 69 | Familial verification | RyR2-  c.11836G＞A | G3946S | Metoprolol  47.5mg | - | 2 |
| 12 | M | 9 | 10 | CPVT | Syncope | 429 | bVT/pVT | - | 71 | WES | RyR2- c.12272C＞T | A4091V | Propranolol  30mg | LCSD | SCD  Aged 16 during physical fight |
| 13 | F | 9 | 10 | CPVT | Syncope | 454 | bVT/pVT | - | 71 | WES | RyR2- c.13786C＞T | P4596S | Propranolol  120mg  Diltiazem  45mg | PM | 9 |
| 14 | M | 7 | 12 | CPVT | Syncope | 413 | bVT/pVT | - | 64 | WES | RyR2-  c.14311G＞A | V4771I | Propranolol  45mg | - | 6 |
| 15 | M | 9 | 14 | CPVT | Syncope | 426 | pVT/VF | - | 60 | WES | RyR2-c.14461G＞A | V4821I | Metoprolol  95mg | PM/RFCA | 14 |
| 16 | F | 7 | 44 | CPVT | Syncope | 414 | pVT | - | 68 | WES | Not related | Not related | Metoprolol  47.5mg  Verapamil  80mg | - | 7 |
| 17 | M | 19 | 19 | CPVT | Palpitation | 405 | pVT | - | 63 | WES | Not related | Not related | Metoprolol  95mg | ICD | 7 |
| 18 | M | 12 | 14 | CPVT | none | 449 | pVT | - | 59 | WES | CASQ2- c.196A＞G | T66A | Propranolol  60mg | - | 6 |
| 19 | F | 8 | 14 | CPVT | CPA | 410 | pVT | - | 70 | Target gene | Not related | Not related | Propranolol  50mg  Diltiazem  180mg | - | 6 |
| 20 | M | 2 | 14 | CPVT | Syncope | 441 | pVT/VF | - | 68 | No | - | - | Metoprolol  47.5mg |  | 9 |
| 21 | M | 8 | 8 | CPVT | Syncope | 426 | bVT/pVT | - | 68 | No | - | - | Metoprolol  23.75mg |  | SCD  Aged 12 during running |
| 22 | M | 12 | 45 | CPVT | Syncope | 408 | bVT/pVT | - | 66 | No | - | - | Metoprolol  47.5mg | - | 11 |
| 23\* | F | 48 | 48 | CPVT | Syncope | 437 | pVT | - | 70 | No | - | - | Metoprolol  75mg | ICD | 14 |
| 24 | M | 21 | 21 | CPVT | Syncope | 405 | bVT/pVT | - | 63 | No | - | - | Metoprolol  95mg | - | 9 |

\*Case 23 was unable to complete exercise stress test due to leg problem. She was diagnosed by electrophysiological study and had recorded exercise-induced pVT in holter.

M: male; F: female; CPA: cardiopulmonary arrest; bVT: bidirectional ventricular arrythmia; pVT: polymorphic ventricular arrhythmia; NC/C: non-compaction / compaction ratio; WES: whole exon sequencing; PM: pace maker; ICD: implantable cardiac defibrillator; LCSD: left cardiac sympathetic denervation; RFCA: radiofrequency catheter ablation; SCD: sudden cardiac death