

**Supplementary Table 1. Athlete Classification**

| Author                           | Training background of patients   | Type of sport/exercise and duration of training                            | Definition of heavy/intense activity | Age (years)  | Gender (male/female)   | Referral status  |
|----------------------------------|---|--|--------------------------------------|--|--|--|
| Dagradi et al. 2020 <sup>1</sup> | <p>Whole sample:</p> <ul style="list-style-type: none"> <li>Competitive athlete (81%)</li> <li>Recreational/noncompetitive (19%) athletes.</li> </ul> <p>Patients with reversible pattern: not specifically mentioned</p> | Not specifically mentioned   | Not defined                          | <p>Whole sample: median 14 years (12-18), range 6-56 years</p> <p>Patients with reversible pattern: not specifically mentioned</p> | 27/33  | All patients were referred by sports medicine physicians due to QT interval prolongation/T wave abnormalities during preparticipation screening  |
| Bains et al. 2023 <sup>2</sup>   | Not specifically mentioned  | Not specifically mentioned   | Not defined                          | <p>Whole sample: 22 ± 14 years</p> <p>Patients with reversible pattern: not specifically mentioned</p>                             | <p>Whole sample: 174/116</p> <p>Patients with reversible pattern: not specifically mentioned</p> | <p>Whole sample:</p> <ul style="list-style-type: none"> <li>Self-referred: 58 (20%)</li> <li>Referred by physician: 232 (80%)</li> </ul> <p>Patients with reversible pattern: not specifically mentioned</p> |
| Pagani et al. 2023 <sup>3</sup>  |   |  |                                      |  |  |  |
| Case 1                           | Military service member   | Swimming and running for 2-3 hours per day                                 | Not defined                          | 22 years   | 1/0  | Referred due to QT interval prolongation during Special Forces training application  |
| Case 2                           | Military service member   | 2,000 meters of swimming 3-4 times a week and 35 miles of running per week | Not defined                          | 20 years   | 1/0  | Referred due to QT interval prolongation during Special Forces training application, examination was conducted following a 36-hour athletic training competition   |
| Case 3                           | Military service member, NCAA Division 1 athlete  | Lacrosse, 3-4 hours of daily exercise                                      | Not defined                          | 21 years   | 0/1  | Referred due to QT interval prolongation during aviation training application  |

|                                     |                     |   |             |               |               |   |
|-------------------------------------|---------------------|---|-------------|---------------|---------------|---|
| Roagna et al. 2024 <sup>4</sup>     | Competitive athlete | Basketball with 11 hours per week of training load and significantly increased in the previous 6 months | Not defined | 16 yr         | Not mentioned | Referred due to QT interval prolongation and T wave abnormalities               |
| Viskin et al. 2010 <sup>5</sup>     | Competitive athlete | Not specifically mentioned  | Not defined | Not mentioned | 0/1           | Referred due to QT interval prolongation during preparticipation screening      |
| Napolitano et al. 2006 <sup>6</sup> | Competitive athlete | Not specifically mentioned  | Not defined | Not mentioned | Not mentioned | Referred due to QT interval prolongation during training period for competition |





**Supplementary Table 3. Additional examinations**

| Author                           | Additional Examination   | Findings  |
|----------------------------------|--|---|
| Dagradi et al. 2020 <sup>1</sup> | <ul style="list-style-type: none"> <li>- Exercise stress test</li> <li>- Holter ECG</li> <li>- Planned for echocardiography</li> </ul>                           | <ul style="list-style-type: none"> <li>- The findings from the Holter are as follows:               <ul style="list-style-type: none"> <li>a. HRmin from 42 ± 5 to 42 ± 5 bpm post-detraining</li> <li>b. Reduced HRmax from 132 ± 16 to 125±22 bpm post-detraining</li> <li>c. Increased HRmean from 71 ± 13 to 72 ± 20 bpm post-detraining</li> <li>d. Reduced QTcmax from 497 ± 32 to 454 ± 23 ms post-detraining</li> </ul> </li> <li>- The findings from the exercise stress test are as follows:               <ul style="list-style-type: none"> <li>a. Reduced HR<sub>basal</sub> from 78 ± 10 to 81 ± 18 bpm post-detraining</li> <li>b. Reduced HR<sub>peak</sub> from 169 ± 11 to 165 ± 21 bpm post-detraining</li> <li>c. Reduced HR<sub>1st-rec</sub> from 133 ± 25 to 139 ± 26 bpm post-detraining</li> <li>d. Reduced QTc<sub>4th-rec</sub> from 465 ± 57 to 422 ± 23 ms post-detraining</li> </ul> </li> <li>- Echocardiography was not performed or reported in this study.</li> </ul> |
| Bains et al. 2023 <sup>2</sup>   | Epinephrine or isoproterenol testing   | <ul style="list-style-type: none"> <li>- Twenty-four patients were misdiagnosed due to overestimation of the QT interval.</li> <li>- Echocardiography was not performed or reported in this study.</li> </ul>   |
| Pagani et al. 2023 <sup>3</sup>  |  |   |
| Case 1                           | <ul style="list-style-type: none"> <li>- Transthoracic echocardiography</li> <li>- Exercise stress test</li> </ul>   | <ul style="list-style-type: none"> <li>- Transthoracic echocardiogram showed no structural abnormalities, and there was no evidence of physiological mechanisms of cardiac adaptation reported in this case.</li> <li>- The stress test was normal, showing appropriate QTc shortening, with a recovery QTc that did not exceed 470 ms at 4 minutes.</li> </ul>   |
| Case 2                           | <ul style="list-style-type: none"> <li>- Transthoracic echocardiography</li> <li>- Cardiac magnetic resonance imaging</li> <li>- Exercise stress test</li> </ul> | <ul style="list-style-type: none"> <li>- Transthoracic echocardiography and cardiac MRI showed no structural pathology, aside from mild LV and LA enlargement consistent with physiological adaptation to high-volume endurance training such as swimming and long-distance running.</li> </ul>   |

|                                     |  |   |
|-------------------------------------|--|---|
|                                     |  | <ul style="list-style-type: none"> <li>- The stress test was normal, showing typical QTc shortening</li> </ul>  |
| Case 3                              | <ul style="list-style-type: none"> <li>- Transthoracic echocardiography</li> <li>- Cardiac magnetic resonance imaging</li> </ul> | Transthoracic echocardiography and cardiac MRI showed no structural abnormalities, and there was no evidence of physiological cardiac adaptation reported in this case.   |
| Roagna et al. 2024 <sup>4</sup>     | <ul style="list-style-type: none"> <li>- Cardiac ultrasound</li> <li>- Holter ECG</li> <li>- Exercise stress test</li> </ul>     | <ul style="list-style-type: none"> <li>- Cardiac ultrasound during the detraining phase showed no structural or functional abnormalities, and no physiological cardiac adaptation was reported in this case.</li> <li>- Holter ECG confirmed the presence of a second dynamic component of ventricular repolarization, resulting in a significantly prolonged QT (QTc max &gt;550 ms). The QTc interval was typically between 375 and 400 ms.</li> <li>- The QTc adaptation during exercise and recovery was preserved, with a recovery QTc of 401 ms at the fourth minute</li> </ul> |
| Viskin et al. 2010 <sup>5</sup>     | Quick standing test  | <ul style="list-style-type: none"> <li>- The patient responded to the test, marked by “Highly abnormal QT-stretching”.</li> <li>- Echocardiography was not performed or reported in this study.</li> </ul>  |
| Napolitano et al. 2006 <sup>6</sup> | Not mentioned in the study   | Echocardiography was not performed or reported in this study.   |

Supplementary Table 4. Detraining protocol

| Author                           | Detraining Protocol                | Follow-up Period   | Clinical Manifestation Before Detraining  | Clinical Manifestation After Detraining  | Additional Interventions Besides Detraining   |
|----------------------------------|------------------------------------|--|---|--|---|
| Dagradi et al. 2020 <sup>1</sup> | A 3-6 months period of detraining. | <ul style="list-style-type: none"> <li>- The specific duration of the follow-up period was not reported.</li> <li>- No cardiac adverse events were recorded during follow-up.</li> <li>- QTc re-prolongation was observed in 7 patients after returning to competitive sports such as rugby and swimming, with some patients experiencing no recurrence during low-intensity sport activities</li> </ul> | <ul style="list-style-type: none"> <li>- Thirty-three patients of cases (reversible pattern) with an average QTc interval of <math>492 \pm 37</math> ms.</li> <li>- Schwartz score at the initial presentation was <math>3.0 \pm 1.2</math></li> <li>- 26 out of 33 patients showed a QTc <math>\geq 470</math> ms.</li> <li>- 29 out of 33 patients had ventricular repolarization abnormalities.</li> <li>- There were no other cardiac-related symptoms or events in any of the patients.</li> </ul> | <ul style="list-style-type: none"> <li>- QTc shortening to <math>423 \pm 25</math> ms.</li> <li>- The Schwartz score decreased (<math>0.06 \pm 0.24</math>) significantly after detraining (<math>P &lt; 0.001</math>).</li> </ul> | 12 out of 33 patients, including those with a cases (reversible pattern), were taking $\beta$ -blockers. The administration of $\beta$ -blockers was given due to worsening LQTS, without waiting for the genetic test results. When the genotype results were negative and the ECG was normal, the $\beta$ -blocker was discontinued. The study does not specify how many remained on $\beta$ -blockers during the post-detraining QTc assessment.   |
| Bains et al. 2023 <sup>2</sup>   | Not mentioned in the study         | <ul style="list-style-type: none"> <li>- The follow-up duration was <math>3 \pm 5</math> years.</li> <li>- All six patients showed normalized QTc intervals after detraining, confirming the initial prolongation was reversible.</li> <li>- No cardiac events or symptoms</li> </ul>  | <ul style="list-style-type: none"> <li>- Whole sample: <ul style="list-style-type: none"> <li>• QTc prolongation following vasovagal syncope.</li> <li>• 44 out of 290 patients were diagnosed with isolated or transient QTc prolongation due to various causes, including panic</li> </ul> </li> </ul>  | Six patients returned to normal QTc after undergoing detraining.   | <ul style="list-style-type: none"> <li>- Whole sample: A total of 232 of 290 patients were initially prescribed <math>\beta</math>-blockers. However, <math>\beta</math>-blocker treatment was discontinued in 194 patients after the removal of the LQTS diagnosis.</li> <li>- The number of patients receiving <math>\beta</math>-blocker therapy at the time of post-detraining QTc assessment was not explicitly reported.</li> <li>- Patients with reversible pattern: not specifically mentioned</li> </ul> |

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|                                 |                              | occurred in the six patients during follow-up.  | <p>attacks, metabolic disturbances, anorexia, drug-induced QT prolongation, sinus arrhythmias, and pregnancy.</p> <ul style="list-style-type: none"> <li>• 5 out of 290 patients had a history of seizures.</li> <li>• 3 out of 290 patients had a history of sudden cardiac arrest.</li> <li>• 3 out of 290 patients had a misdiagnosis of Jervell and Lange-Nielsen Syndrome.</li> <li>• Patients with reversible pattern: not specifically mentioned</li> </ul> |   |  |
| Pagani et al. 2023 <sup>3</sup> |                              |   |  |   |  |
| Case 1                          | 1-month period of detraining | <ul style="list-style-type: none"> <li>- The follow-up duration was 5 months.</li> <li>- No cardiac adverse events were reported during follow-up.</li> <li>- During follow-up, the QTc interval normalized to</li> </ul> | <ul style="list-style-type: none"> <li>- One patient with a QTc interval of 480 ms.</li> <li>- Reported having 1 episode of syncope at the age of 13.</li> <li>- There were no other cardiac-related symptoms or events.</li> </ul>  | One patient with a QTc interval had it reduced to 440 ms. | The patient was not taking any medication. |

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|--------|-----------------------------|--|---|---|--|
|        |                             | <p>440 ms after one month of detraining and remained within the normal range (440–450 ms) after resuming swimming or running.</p> <ul style="list-style-type: none"> <li>- The patient resumed 2–3 hours/day of swimming or running and remained asymptomatic; stress test normal.</li> </ul>  |   |   |  |
| Case 2 | 6-week period of detraining | <ul style="list-style-type: none"> <li>- The follow-up duration was 15 weeks.</li> <li>- No cardiac adverse events were reported during follow-up.</li> <li>- During follow-up, QTc reduced to 440–450 ms after 6-week detraining; stable on follow-up.</li> <li>- During follow up, the patient returned to running (35 miles/week) and swimming also remained</li> </ul> | <ul style="list-style-type: none"> <li>- One patient with a QTc interval of 486 ms.</li> <li>- There were no other cardiac-related symptoms or events.</li> </ul> | One patient with a QTc interval had it reduced to 440-450 ms. | The patient was not taking any medication. |

|        |                                       |   |   |  |   |
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|        |                                       | asymptomatic;<br>stress test<br>normal  |   |  |   |
| Case 3 | A 2-3 months<br>period of detraining. | <ul style="list-style-type: none"> <li>- The follow-up duration was 3 years (2019-2022).</li> <li>- No cardiac adverse events were reported during follow-up.</li> <li>- During follow-up, the QTc interval normalized (420–440 ms) after 2–3 months of detraining, with no QT prolongation observed during stress testing.</li> <li>- The patient resumed daily NCAA-level training, remained asymptomatic, and had a stable QTc interval (410 ms in 2022).</li> </ul> | <ul style="list-style-type: none"> <li>- One patient with a QTc interval of 475 ms.</li> <li>- There were no other cardiac-related symptoms or events.</li> </ul> | <ul style="list-style-type: none"> <li>- Not detect any arrhythmias.</li> <li>- One patient with a QTc interval had it reduced to 420 ms on an ECG post retraining.</li> </ul> | Patient was taking propranolol due to QTc prolongation. |

|                                       |  |  |   |  |   |
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| <p>Roagna et al. 2024<sup>4</sup></p> | <p>A complete 6-month detraining period.</p> | <ul style="list-style-type: none"> <li>- The follow-up duration was 6 months.</li> <li>- No cardiac adverse events were reported during follow-up.</li> <li>- During follow-up, QTc normalized (from &gt;550 ms on Holter to 401 ms on ECG); repolarization abnormalities resolved except transient U-wave post-HR spike; LV function and electromechanical parameters preserved.</li> <li>- Return to play permitted with reduced load (6 h/week); ECG normal at 3-month follow-up</li> </ul> | <p>One patient exhibited the following ECG findings:</p> <ul style="list-style-type: none"> <li>- Notched T waves in lead V2-V3 and late T wave peaks in other leads.</li> <li>- Mild QTc prolongation in lead DII (455 ms) and severe QTc prolongation in leads V2-V3 (&gt;550 ms on Holter ECG).</li> <li>- A second dynamic component of ventricular repolarization, especially after sudden heart increases.</li> </ul> | <ul style="list-style-type: none"> <li>- Normalized QTc and resolution of morphological abnormalities on resting ECG (QTc in lead DII reduced to 401 ms).</li> <li>- QTc mostly ranged between 375-400 ms on Holter ECG</li> <li>- Preserved QTc adaptation during exercise and recovery (4<sup>th</sup> minute recovery QTc: 401 ms).</li> <li>- Echocardiography showed preserved left ventricular ejection fraction (LVEF 62%), global longitudinal strain (-23%), and improved electromechanical dispersion parameters.</li> </ul> | <p>Not mentioned in the study</p>   |
| <p>Viskin et al. 2010<sup>5</sup></p> | <p>4-month period of detraining</p>          | <ul style="list-style-type: none"> <li>- The follow-up duration was 4 months.</li> <li>- No cardiac adverse events were reported during follow-up.</li> </ul>  | <ul style="list-style-type: none"> <li>- There were no other cardiac-related symptoms or events</li> <li>- QTc interval ranging from 461 to 473 ms (97<sup>th</sup> to 99<sup>th</sup> percentile for healthy women).</li> <li>- A positive response to the quick standing</li> </ul>   | <p>The QTc interval was partially but significantly reduced to 403 ms.</p>   | <p>Only one patient was reported to have post-detraining QTc measurements while receiving <math>\beta</math>-blocker therapy.</p> |

|                                     |                              |  |  |   |                             |
|-------------------------------------|------------------------------|--|--|---|-----------------------------|
|                                     |                              | <ul style="list-style-type: none"> <li>- During follow-up, QTc partially normalized (461–473 ms to lower range); T-wave abnormalities improved post-detraining.</li> </ul>   | test indicating the presence of LQTS symptoms.   |   |                             |
| Napolitano et al. 2006 <sup>6</sup> | 5-month period of detraining | <ul style="list-style-type: none"> <li>- The follow-up duration was 5 months.</li> <li>- No cardiac adverse events were reported during follow-up.</li> <li>- During follow-up, QTc and T-wave abnormalities normalized after detraining and the initial ECG changes suggestive of LQTS resolved.</li> </ul> | <ul style="list-style-type: none"> <li>- Patients with a prolonged QTc interval.</li> <li>- Changes in the morphology and duration of cardiac repolarization.</li> </ul> | Patient showed completely normal repolarization after detraining. | Not mentioned in the study. |

**Supplementary Table 5. Exercise-Induced QT Prolongation and Detraining Outcomes**

| Study                            | Population  | Baseline QT Interval   | Genetic Testing   | Detraining Outcomes   | Schwartz Score   | Key Conclusions  |
|----------------------------------|---|--|---|---|--|--|
| Dagradi et al. 2020 <sup>1</sup> | 199 patients: 121 genotype-positive LQTS, 78 genotype-negative. 33 cases exhibited reversible ECG abnormalities after detraining. | QTc baseline: 492 ± 37 ms (cases group).                               | Negative in 78 genotype-negative patients.  | QTc shortened significantly after detraining to 423 ± 25 ms. Holter monitoring showed QTc shortening from 497 ± 32 ms to 454 ± 23 ms. | Schwartz scores decreased significantly from 3.0 ± 1.2 to 0.06 ± 0.24 post-detraining. | QT prolongation in some athletes is reversible after detraining, distinguishing it from congenital LQTS.                   |
| Bains et al. 2023 <sup>2</sup>   | 290 referred patients; 6 misdiagnosed with exercise-induced QT prolongation; mean age 22 ± 14.                                    | Referral QTc: 504 ± 39 ms; corrected QTc post-evaluation: 427 ± 25 ms. | 68 tested positive for a variant, but specific cases had negative genetic findings. | QTc normalization occurred post-detraining (specific values not mentioned).   | Not mentioned in the study.  | Exercise-induced QT prolongation may lead to misdiagnosis; detraining helps clarify the diagnosis and avoid overtreatment. |
| Pagani et al. 2023 <sup>3</sup>  | 3 military service members with exercise-induced QT prolongation.   | QTc baseline: Case 1 – 480 ms; Case 2 – 486 ms; Case 3 – 475 ms.       | Negative for all cases.   | QTc normalized after detraining: Case 1 – 440 ms (1 month); Case 2 – 440-450 ms (6 weeks); Case 3 – 420-440 ms (2-3 months).          | Not mentioned in the study.  | QTc prolongation resolved within 1–2 months of detraining; no recurrence even after return to physical activity.           |
| Roagna et al. 2024 <sup>4</sup>  | 1 competitive basketball player, 16 years old, with increased training load.  | Mild QTc prolongation (455 ms in DII); Holter QTc max >550 ms.         | Negative genetic testing.   | QTc normalized after 6 months of detraining to 401 ms; T-wave abnormalities resolved, and exercise stress showed recovery.            | Not mentioned in the study.  | Intense exercise can cause ventricular repolarization abnormalities; detraining helps differentiate from true LQTS.        |

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| Viskin et al. 2010 <sup>5</sup>     | 1 competitive athlete with QTc prolongation during screening.                | Baseline QTc: 461–473 ms.    | Negative genetic testing.   | QTc normalized after 4 months of detraining to 403 ms.  | Not mentioned in the study. | Customized management, including detraining, may allow athletes to safely return to sports without overtreatment. |
| Napolitano et al. 2006 <sup>6</sup> | 1 competitive athlete referred for QTc prolongation during intense training. | Baseline QTc: 511 ms in DII. | Not mentioned in the study. | QTc shortened significantly to 392 ms after detraining. | Not mentioned in the study. | The interpretation of QT interval normalization post detraining lacks scientific evidence at the time of writing. |

## References

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