## T1 mapping tables

**Table 3c-i.1**. Overview of the T1 mapping indices. ECV – extracellular volume fraction, Ht – hematocrit, ECS – extracellular space, GCAs – gadolinium contrast agent, ROI – region of interest, CMR – cardiovascular magnetic resonance.

|  |  |  |  |
| --- | --- | --- | --- |
| **Index** | **Native T1** | **Postcontrast T1** | **ECV** |
| Measurement | Direct myocardial T1 measurement | Direct myocardial T1 measurement | Calculation based on T1 measurement of   * native and postcontrast myocardium * native and postcontrast blood pool   and Hematocrit (Ht). |
| Calculation | Exponential fit of data-points obtained during T1 relaxation | as for native T1 | (1/T1postcontrastMyo - 1/T1nativeMyo)  ECV= (1-Ht) \* \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  (1/ T1postcontrastBlood - 1/T1nativeBlood) |
| Main source of influence | Intracellular and extracellular compartment of native myocardium | Gadolinium effects in extracellular compartment | Gadolinium effects in extracellular compartment |
| Histological relationships | * Intra- and extracellular edema * Interstitial fibrosis * Scar (replacement fibrosis) * Amyloid infiltration * Iron accumulation\* * Lipid infiltration\*   \* = causing reduction of T1 | Expanded extracellular space:   * Replacement fibrosis * Interstitial fibrosis * Extracellular edema * Amyloid infiltration | Expanded extracellular space:   * Replacement fibrosis * Interstitial fibrosis * Extracellular edema * Amyloid infiltration |
| Strengths | 1. Simplicity  * Single breath-hold acquisition * Contrast-agent free  1. Reproducible postprocessing (based on septal ROI) 2. Normal ranges and discrimination between health and disease 3. Outcome data available | 1. Simplicity  * Single breath-hold acquisition  1. Close relationship with ECS by tracking of the effects of the GCAs 2. Allows assessment of regional heterogeneity | 1. Close relationship with ECS by tracking of the effects of the GCAs 2. Allows assessment of regional heterogeneity 3. Outcome data available |
| Weaknesses and limitations | 1. Normal values sequence specific 2. Diagnostic accuracy sequence dependent (T2 sensitive) 3. Nonspecific for multiple underlying abnormalities 4. Assessment of regional heterogeneity possible in artefact free images | 1. Difficult standardization:   * No normal ranges * Intra and inter-individual variations in renal clearance * Differences between GCAs  1. Reliance on GCAs 2. Reliance on T1 accuracy | 1. Reliance on several measurements obtained ~15 min apart 2. Accumulation of errors with dispersion of values 3. Difficult standardization:    * Dispersion of values    * Intra and inter-individual variations in renal clearance    * Differences between GCAs 4. Nonspecific for multiple underlying abnormalities 5. Requires GCAs 6. Requires contemporaneous hematocrit 7. Reliance on T1 accuracy (difficult in water rich myocardium) |
| Possible applications | * Screening for subclinical disease * Risk stratification * Grading of disease severity * Monitoring treatment response * Contrast free CMR | * Marker of expanded extracellular space * Assessment of regional heterogeneity | * Marker of expanded extracellular space * Risk stratification * Grading of disease severity |

**Table 3c-i.2**. **Histological correlations with T1 mapping indices in various cardiac conditions.** Types of sequences and a staining method used, as well as a number of patients included, is also reported. Discriminative focus on replacement vs. interstitial fibrosis is a paramount factor influencing the diversity of observed relationships; whereas some authors steered away from the inclusion of replacement fibrosis/LGE affected areas in histological CVF (or accounted for them separately)(1-4)**,** or all-inclusive(5-7). IHD – ischaemic heart disease, VAST variable sampling of k-space in time, NICM – non-ischemic cardiomyopathy, HFpEF – heart failure with preserved ejection fraction, DCM – dilated cardiomyopathy, FLASH-IR - fast low-angle shot – inversion recovery. \*shMOLLI is a MOLLI (5(1)1(1)1 (FA 35°) variant utilizing a conditional reconstruction algorithm.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Collagen volume fraction%** | **N of patients (cardiac disease)** | **Sequence** | **GCAs (dose and type)** | **T1 Index** | | **Staining** | | **Pearson r (Sig)** | |
| ***Heart failure*** | |  |  | |  | |  | |  |
| Iles(1) | 9 (IHD) | VAST | (0.2 mmol/kg gadopentetate dimeglumine) | Postcontrast T1 | | picrosirius red | | -0.7(0.03) | |
| Sibley(8) | 47 (NICMs) | Look-Locker | (0.2 mmol/kg gadodiamide) | Postcontrast T1 | | Masson trichrome | | −0.57 (<0.001) | |
| [Mascherbauer](http://www.ncbi.nlm.nih.gov/pubmed/?term=Mascherbauer%20J%5BAuthor%5D&cauthor=true&cauthor_uid=24036385) (9) | 9 (HFpEF) | FLASH-IR | (0.2 mmol/kg gadobutrol) | Postcontrast T1 | | Masson Trichrome/Congo-red | | -0.98 (<0.01) | |
| Miller(5) | 6 (IHD) | MOLLI 3(3)3(3)5(FA 35°) | (0.2 mmol/kg (gadopentetate dimeglumine) | Native T1 | | picrosirius red | | 0.199 (0.437) | |
| Postcontrast T1 | | −0.21 (0.69) | |
| ECV (bolus) | | 0.945 (0.004) | |
| Aus dem Siepen(6) | 45 (DCM) | MOLLI 3(3)3(3)5(FA 35°) | (0.2 mmol/kg gadopentetate dimeglumine) | ECV (bolus) | | Acid Fuchsin Orange-G | | 0.85 (0.01) | |
| Iles(4) | 4 (1 IHD, 3 DCM) | VAST | (0.2 mmol/kg gadopentetate dimeglumine) | LGE | | Masson Trichrome | | 0.73 (<0.001) | |
| Postcontrast T1 | | -0.64 (0.002) | |
| Kammerlander(2) | 36 (mixed group) | MOLLI 5(3)3 (FA 35°) for native acquisition  MOLLI 4(1)3(1)2(FA 35°) for postcontrast acquisition | (0.1 mmol/kg of gadobutrol) | ECV (bolus) | | Tissue FAXS | | 0.493 (<0.002) | |
| ***Aortic stenosis*** | |  |  | |  | |  | |  |
| Flett(10) | 18 | FLASH-IR | (0.2 mmol/kg gadoterate meglumine) | ECV (EQ) | | picrosirius red | | 0.94 (R2= 0.89, 0.001) (Tau=0.71) | |
| Bull(3) | 19 | \*shMOLLI |  | Native T1 | | picrosirius red | | 0.655 (0.002) | |
| Fontana(11) | 18 | FLASH-IR | (0.2 mmol/kg gadoterate meglumine) | ECV (EQ) | | picrosirius red | | 0.78 (R2=0.589, p<0.01) | |
|  |  | \*shMOLLI | 0.83 (R2=0.685, <0.01) | |
| White(12) | 18 | \*shMOLLI | (0.2 mmol/kg gadoterate meglumine) | ECV (bolus)  ECV (EQ) | | picrosirius red | | 0.83 (R2=0.69, <0.01)  0.84 (R2=0.71, <0.01) | |
| de Meester de Ravenstein(7) | 12 | MOLLI 3(3)3(3)5 (FA35°) | (0.2 mmol/kg gadobutrol) | Native T1 | | picrosirius red | | -0.15 (0.64) | |
|  | Postcontrast T1 | | -0.64 (0.024) | |
|  | ECV | | 0.91 (0.001) | |
| Lee(13) | 10 | MOLLI 3(3)3(3)5(FA35°) |  | Native T1 | | picrosirius red | | 0.77 (<0.01) | |
| ***Hypertrophic cardiomyopathy*** | |  |  | |  | |  | |  |
| Flett(10) | 8 | FLASH-IR | (0.2 mmol/kg gadoterate meglumine) | ECV | | picrosirius red | | R2=0.62(0.08), Tau=0.52 | |
| Iles(4) | 8 | VAST | (0.2 mmol/kg gadopentetate dimeglumine) | Postcontrast T1 | | Masson-trichrome | | -0.71 (0.01) | |

**Table 3c-i.3**. **Intra, interobserver and interstudy variability reported for various sequences and field strengths.**

Septal ROIs (14-16), SAX ROIs for others. Results are reported as Bland-Altman plots: MD±SD (or ±SD) and CoV in brackets when available. AS: aortic stenosis. shMOLLI is a MOLLI (5(1)1(1)1 (FA 35°) variant utilizing a conditional reconstruction algorithm.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Dabir**(14) | | | **Ferreira** (15) | **Dass** (16) | **Rogers**(17) | | | | | | **Von Knobelsdorff**(18) | **Liu**(19) | **Messroghli**(20) | **Singh**(21) | | **Pica**(22) | | **Weingärtner**(23) | |
| **Magnetic field (T)** | 1.5/3.0 | | | 1.5 | 3.0 | 1.5 | | | 3.0 | | | 3.0 | 3.0 | 1.5 | 3.0 | | 1.5 | | 3.0 | |
| **N** | 10 | | | 42 | 8 | 56 | | | 44 | | | 20 | 24 | 15 | 10 | | 21 | | 20 | |
| **Population** | Healthy volunteers | | | Healthy volunteers and patients | Healthy volunteers and patients | Patients | | | Patients | | | Healthy volunteers | Healthy volunteers | Healthy volunteers | AS | | Fabry disease | | Healthy volunteers | |
| **T1 index** | Native T1 | | Post T1 | Native T1 | Native T1 | Native T1 | Post T1 | Lambda | Native T1 | Post T1 | Lambda | Native T1 | ECV | Native T1 | Native T1 | Post T1 | Native T1 | | Native T1 | Post T1 |
| **Sequence** | MOLLI 3(2)3(2)5 (FA 50º) | | | \*shMOLLI | \*shMOLLI | MOLLI 3(2)3(2)5 (FA 50º) | | | | | | MOLLI 3(3)3(3)5 (FA 35º) | MOLLI 3(3)5 (FA 35º) | MOLLI 3’3’5 (FA 50º) | MOLLI 3(3)3(3)5 (FA 50º) | | MOLLI 5(3)3 (FA35º) | \*shMOLLI | MOLLI 3(3)5 (FA 35º) | MOLLI 4(1)3(1)2 (FA 35º) |
| SAPPHIRE | |
| SASHA | |
| **Inter-observer V** | 1.3±6.8 (6.1%) | -5.9±9.8 (16.2%) | | ±5.6 | ±24 | 1.5±19 (4.3%) | 6.3±52 (4.3%) | 13 ± 19 (7.2%) | 3 ± 13  (1.2%) | −6 ± 15  (3.2%) | 17 ± 20  (5.1%) | 0.5±20.2 | -6±17 (6.4%) | -1.1±8.9 (0.9%) | -2.3±3.7 (0.34%) | 0±5 (2.31) | (1.1%) | -0.8± 2.9% (1.4%) | 11.3 | 2.8 |
| 13.0 | 5.3 |
| 8.8 | 5.3 |
| **Intra-observer V** | 2.1±4.3 (5.2%) | -4.8±7.2 (12.6%) | | ±5.6 |  | 3±11 (1.1%) | 5±12 (3.1%) | 14 ± 9  (4.1%) | 0.3 ± 15  (1.4%) | 6.2 ± 71  (2.8%) | 19 ± 8  (9.1%) | 4.6±18.3 | 7±06 (2.2%) | 2.6±6.7 (0.7%) | 0.18±5.6 (0.5%) | -1± 4 (1.8%) | (1.2%) | -0.3± 2.2% (1.5%) | 7.1 | 3.6 |
| 5.1 | 4.1 |
| 3.3 | 3.2 |
| **Inter-study V** |  |  | |  |  | 2.4 ± 9.2  (1.2%) | −8 ± 54  (9.0%) | 0.017 ± 0.021  (4.2%) | −1.5 ± 12  (3.6%) | 19 ± 65  (12%) | 0.016 ± 0.018  (3.5%) |  |  |  | -8.2± 19.3 (1.77%) | 2±0.15 (6.5%) | (1.5%) | -0.3±2.2% (0.8%) |  | |

**Table 3c-i.4. Overview of studies reporting normative ranges for T1 mapping indices**. Studies included if n>50 subjects. Number of participants per group, mean values (mean±SD) are reportedfor the type of sequence, T1 index and field strength, T1 mapping indices. Postcontrast T1measurements were typically obtained > 15 min after contrast administration. \*shMOLLI is a MOLLI (5(1)1(1)1 (FA 35°) variant utilizing a conditional reconstruction algorithm.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Study (n = participants)** |  |  |  | **1.5 T** |  | **3.0 T** |  |
|  | **Sequence** | **GCAs (dose and type)** | **T1 index** | **Myocardium** | **Blood** | **Myocardium** | **Blood** |
| Piechnik(24) (n= 342) | \*shMOLLI |  | Native T1 (ms) | 962±25 | 1535±76 |  |  |
| Dabir(14) (n=102) | MOLLI 3(2)3(2)5 (FA 50º) | (0.1-0.2 mmol/kg gadobutrol) | Native T1 (ms) | 950 ± 21 | 1551 ± 115 | 1052 ± 23 | 1736 ± 139 |
| ECV (%) | 25±4 |  | 26±4 |  |
| Liu(25) (n=1231) | MOLLI 3(3)3(3)5(FA 35°) | (0.15 mmol/kg gadopentetate dimeglumine) | Native T1 (ms) | 977 ± 42 |  |
| ECV% | 26.9±2.8 |
| Von Knobelsdorff(18) (n=60) | MOLLI 3(3)3(3)5(FA 35°) |  | Native T1 (ms) |  | 1159±≈73 |

**Table 3c-i.5. Proof of concept studies using T1 mapping in health and disease.** Studies included if n>25 subjects/patients’ group. Number of participants per group, mean values (mean±SD) are reportedfor disease entity, the type of sequence, T1 index and field strength, including effect size as a measure of dispersion observed in healthy subjects, as well as the Cohen’s d index. The order relates to the order referencing. \*shMOLLI is a MOLLI (5(1)1(1)1 (FA 35°) variant utilizing a conditional reconstruction algorithm; \*\*merged results from 1.5 and 3.0 T field strength.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | **Health (n)** | | **Disease (n)** | |  |
|  | **Sequence (dose and type of gadolinium contrast agent)** | **Myocardial T1 index** | | | | **Effect size** **(Cohen’s d)** |
|  | | 1.5 T | 3.0 T | 1.5 T | 3.0 T |  |
| **Amyloidosis (ATTR)** | | **Native T1 (ms)** | | | |  |
| Fontana(26) | \*shMOLLI | 967 ±34  (n=52) |  | 1097±43  (n=85) |  | 3.5 |
|  |  | **Postcontrast T1 (ms)** | | | |  |
| **Amyloidosis (AL)** | | **Native T1 (ms)** | | | |  |
| Banypersad(27) | \*shMOLLI | 954±34  (n=54) |  | 1080±87  (n=100) |  | 1.9 |
| Karamitsos(28) | \*shMOLLI | 958±20  (n=36) | 1140± 61  (n=53) | 3.5 |
| Fontana(26) | \*shMOLLI | 967 ±34  (n=52) | 1130±68  (n=79) | 3.0 |
|  |  | **ECV (%)** | | | |  |
| Banypersad(27) | \*shMOLLI  (0.1 mmol/kg gadoterate meglumine) | 25±2  (n=54) |  | 44±12  (n=100) |  | 2.3 |
| Fontana(26) | shMOLLI  (0.1 mmol/kg gadoterate meglumine) | 27±3  (n=50) | 52±7  (n=20) | 4.3 |
| **Aortic stenosis** | | **Native T1 (ms)** | | | |  |
| Bull(3) | \*shMOLLI | 944±16  (n=33) |  | 971±39 (n=109) |  | 0.9 |
| Mahmod(29) | \*shMOLLI |  | 1168±27  (n=16) |  | 1196 ± 47  (n=26) | 0.7 |
| Lee(13) | MOLLI 3(3)3(3)5 (FA 35°) |  | 1169±21 (n=15) |  | 1214±45 (n=62) | 1.3 |
| Singh(21) | MOLLI 3(3)3(3)5 (FA 50°) | 1092±35 (n=22) | 1103±33 (n=50) | 0.32 |
|  |  | **ECV (%)** | | | |  |
| Singh(21) | MOLLI 3(3)3(3)5 (FA 50°)  (0.15 mmol/kg of gadobutrol) |  | 24±2 (n=22) |  | 25±3 (n=50) | 0.4 |
| Fontana(26) | \*shMOLLI  (0.1 mmol/kg gadoterate meglumine) | 27±3  (n=50) |  | 31±5  (n=50) |  | 1.0 |
| **DCM (non-ischemic)** | | **Native T1 (ms)** | | | |  |
| Puntmann(30) | MOLLI 3(2)3(2)5 (FA 50º) |  | 1070±55 (n=30) |  | 1239±57 (n=27) | 3.0 |
| Puntmann(31) | MOLLI 3(2)3(2)5 (FA 50º) | 1055±22 (n=47) | 1115±37 (n=82) | 1.9 |
| Aus dem Siepen(6) | MOLLI 3(3)5 (FA 35°) | 1020±40  (n=56) |  | 1056±62  (n=29) |  | 0.9 |
|  |  | **Post-contrast T1(ms)** | | | |  |
| Puntmann(30) | MOLLI 3(2)3(2)5 (FA 50º)  (0.2 mmol/kg of gadobutrol |  | 440±58 (n=30) |  | 355±44 (n=27) | 1.6 |
| Aus dem Siepen(6) | MOLLI 3(3)5 (FA 35°)  (0.2 mmol/kg gadopentetate dimeglumine) | 442±43  (n=56) |  | 420±45  (n=29) |  | 0.5 |
|  |  | **ECV (%)** | | | |  |
| Puntmann(30) | MOLLI 3(2)3(2)5 (FA 50º)  (0.2 mmol/kg of gadobutrol) |  | 27±10 (n=30) |  | 41±10 (n=27) | 1.4 |
| Aus dem Siepen(6) | MOLLI 3(3)5 (FA 35°)  (0.2 mmol/kg gadopentetate dimeglumine) | 23±3  (n=56) |  | 27±4  (n=29) |  | 1.1 |
| Puntmann(31) | MOLLI 3(2)3(2)5 (FA 50º)  (0.2 mmol/kg of gadobutrol) |  | 27±9 (n=47) |  | 40±9  (n=82) | 1.4 |
| Ugander(32)  LGE-  LGE+ | MOLLI 3(3)5 (FA 35°)  (0.15 mmol/kg gadopentetate dimeglumine) | (n=11)  25±3 |  | (n=30)  26±3  37±6 |  | 0.3  2.6 |
| **Hypertension** | | **Native T1 (ms)** | | | |  |
| Hinojar(33) | MOLLI 3(2)3(2)5 (FA 50º) |  | 1044±18 (n=23) |  | 1058±29 (n=69) | 0.6 |
| Treibel(34) | \*shMOLLI | 965±38  (n=50) |  | 955±30 (n=46) |  | 0.3 |
|  |  | **Post-contrast T1 (ms)** | | | |  |
| Hinojar(33) | MOLLI 3(2)3(2)5 (FA 50º)  (0.2 mmol/kg of gadobutrol) |  | 446±70 (n=23) |  | 429±60 (n=69) | 0.3 |
| Treibel(34) | \*shMOLLI  (0.1 mmol/kg of gadoterate meglumine) | 618±33  (n=50) |  | 578±37  (n=46) |  | 1.1 |
|  |  | **ECV (%)** | | | |  |
| Hinojar(33) | MOLLI 3(2)3(2)5 (FA 50º)  (0.2 mmol/kg of gadobutrol) |  | 24±6  (n=23) |  | 24±4  (n=69) | 0 |
| Treibel(34) | \*shMOLLI  (0.1 mmol/kg of gadoterate meglumine) | 26±2  (n=50) |  | 27± 3  (n=46) |  | 0.5 |
| **Hypertrophic cardiomyopathy** | | **Native T1 (ms)** | | | |  |
| Puntmann(30) | MOLLI 3(2)3(2)5 (FA 50º) |  | 1070±55 (n=30) |  | 1254±43 (n=25) | 3.7 |
| Dass(16) | \*shMOLLI | 1178±13 (n=12) | 1209±28 (n=28) | 1.4 |
| Hinojar(33) | MOLLI 3(2)3(2)5 (FA 50º) | 1044±18 (n=23) | 1169±41 (n=95) | 3.9 |
|  |  | **Post-contrast T1** | | | |  |
| Puntmann(30) | MOLLI 3(2)3(2)5 (FA 50º)  (0.2 mmol/kg of gadobutrol) |  | 440±58 (n=30) |  | 363±63 (n=25) | 1.3 |
| Hinojar(33) | MOLLI 3(2)3(2)5 (FA 50º)  (0.2 mmol/kg of gadobutrol) | 446±70 (n=23) | 379±47 (n=95) | 1.3 |
| Ellims(35) | VAST (FA 25°)  (0.2 mmol/kg gadopentetate dimeglumine) | 545±49  (n=25) |  | 483+83 (n=139) |  | 0.9 |
| Ellims(36) | VAST (FA 25°)  (0.2 mmol/kg gadopentetate dimeglumine) | 561 ± 47  (n=25) | 498 ± 80 (n=76) | 0.96 |
|  |  | **ECV (%)** | | | |  |
| Puntmann(30) | MOLLI 3(2)3(2)5 (FA 50º)  (0.2 mmol/kg of gadobutrol) |  | 27±9 (n=30) |  | 41±12  (n=25) | 1.3 |
| Hinojar(33) | MOLLI 3(2)3(2)5 (FA 50º)  (0.2 mmol/kg of gadobutrol) | 24±6 (n=23) |  | 31±6 (n=95) | 1.2 |
| Ho CY(37) | Look-Locker  (0.15 mmol/kg gadopentetate dimeglumine) | 27±1  (n=11) |  | 36±1  (n=37) |  | 9 |
| **HCM G+ relatives** | | **Native T1 (ms)** | | | |  |
| Hinojar(33) | MOLLI 3(2)3(2)5 (FA 50º) |  | 1044±18 (n=23) |  | 1105±17 (n=23) | 3.4 |
|  |  | **Postcontrast T1 (ms)** | | | |  |
| Hinojar(33) | MOLLI 3(2)3(2)5 (FA 50º)  (0.2 mmol/kg of gadobutrol) |  | 446±70 (n=23) |  | 434±67 (n=23) | 1.7 |
|  | | **ECV%** | | | |  |
| Ho CY(37) | Look-Locker  (0.15 mmol/kg gadopentetate dimeglumine) | 27±1  (n=11) |  | 33±1  (n=29) |  | 6 |
| Hinojar(33) | MOLLI 3(2)3(2)5 (FA 50º)  (0.2 mmol/kg of gadobutrol) |  | 24±6 (n=23) |  | 25±4 (n=23) | 2.0 |
| **Anderson-Fabry disease** | | **Native T1 (ms)** | | | |  |
| Sado(38) | \*shMOLLI | 968±32  (n=67) |  | 882±47  (n=44) |  | 2.3 |
| Pica(22) | \*shMOLLI | 968±32  (n=63) | 853±50  (n=63) | 2.7 |
| **Iron overload** | | **Native T1 (ms)** | | | |  |
| Sado(39) | \*shMOLLI  (0.1 mmol/kg gadoterate meglumine) | 968±32  (n=67) |  | 827±135 (n=88) |  | 1.4 |
|  | | | | | | |
| **Acute viral myocarditis** | | **Native T1 (ms)** | | | |  |
| Hinojar(40) | MOLLI 3(2)3(2)5 (FA 50º) | 940±20  (n=18) | 1045±23 (n=22) | 1064±37 (n=23) | 1189±52 (n=38) | 3.7/3.4 |
| Ferreira(41) | \*shMOLLI | 946±23  (n=45) |  | 1010±65 (n=50) |  | 1.4 |
|  |  | **Post contrast T1 (ms)** | | | |  |
| Hinojar(40) | MOLLI 3(2)3(2)5 (FA 50º)  (0.2 mmol/kg of gadobutrol)  Acute (N=61)  Chronic (N=67) | (n=18)  422±68 | 442±68 | (n=23)  373±42  383±43 | (n=38)  397±62  426±73 | 0.5/0.3  0.4/0.2 |
| **Chronic viral myocarditis** | | **Native T1 (ms)** | | | |  |
| Radunski(42) | MOLLI 3(3)5 (FA 35°) | 1051±37  (n=21) |  | 1098±57 (n=114) |  | 0.9 |
| Hinojar(40) | MOLLI 3(2)3(2)5 (FA 50º) | 940±20  (n=18) | 1045±23 (n=22) | 995±19  (n=33) | 1099±22 (n=34) | 2.2/2.2 |
| Bohnen(43) | MOLLI 3(3)5 (FA 35°) | / |  | 1128±~47  (n=31) |  |  |
|  |  | **Postcontrast T1 (ms)** | | | |  |
| Radunski(42) | MOLLI 3(3)5 (FA 35°)  (0.075 mmol/kg gadobenate dimeglumine) | 579±45  (n=21) |  | 555±~61  (n=114) |  | 0.4 |
| Hinojar(40) | MOLLI 3(2)3(2)5 (FA 50º)  (0.2 mmol/kg of gadobutrol) | 422±68  (n=18) | 442±68 (n=22) | 383±43  (n=33) | 426±73 (n=34) | 0.8/0.3 |
| Bohnen(43) | MOLLI 3(3)5 (FA 35°)  (0.075 mmol/kg gadobenate dimeglumine) |  |  | 572±~57  (n=31) |  |  |
|  |  | **ECV (%)** | | | |  |
| Radunski(42) | MOLLI 3(3)5 (FA 35°)  (0.075 mmol/kg gadobenate dimeglumine) | 25±3  (n=21) |  | 31±~4  (n=114) |  | 1.7 |
| Bohnen(43) | MOLLI 3(3)5 (FA 35°)  (0.075 mmol/kg gadobenate dimeglumine) |  | 31±~6  (n=31) |  |
| **Systemic inflammatory diseases** | | **Native T1 (ms)** | | | |  |
| Puntmann(44) | MOLLI 3(2)3(2)5 (FA 50º) |  | 1056±27 (n=21) |  | 1152±46 (n=33) | 2.5 |
| Hinojar (45) | MOLLI 3(2)3(2)5 (FA 50º) | 1057 ± 23  (=n46) | 1176 ± 55  (n=76) | 2.8 |
| Ntusi(46) | \*shMOLLI | 961±18  (n=39) |  | 973±27 (n=39) |  | 0.5 |
| Holloway(47) | \*shMOLLI | 962±18  (n=39) | 965±~35 (n=129) | 0.8 |
|  |  | **Postcontrast T1 (ms)** | | | |  |
| Puntmann(44) | MOLLI 3(2)3(2)5 (FA 50º)  (0.2 mmol/kg of gadobutrol) |  | 454±53  (n=21) |  | 411±61 (n=33) | 0.7 |
| Ntusi(46) | \*shMOLLI  (0.15 mmol/kg gadopentetate dimeglumine) | 468±32  (n=39) |  | 450±40  (n=39) |  | 0.5 |
|  |  | **ECV (%)** | | | |  |
| Puntmann(44) | MOLLI 3(2)3(2)5 (FA 50º)  (0.2 mmol/kg of gadobutrol) |  | 26±5  (n=21) |  | 30±6  (n=33) | 0.7 |
| Ntusi(46) | \*shMOLLI  (0.15 mmol/kg gadopentetate dimeglumine) | 28±2  (n=39) |  | 30±3  (n=39) |  | 0.6 |
| **Chemotherapy** | | **ECV (%)** | | | |  |
| Neilan(48) | Look-Locker  (0.15 mmol/kg gadodiamide) | 28±2  (n=15) |  | 30±3  (n=42) |  | 0.8 |
|  | |  |  |  |  |  |
| **Congenital heart disease** | | **ECV (%)** | | | |  |
| Broberg(49)\*\* | Look-Locker  (0.15 mmol/kg gadodiamide) | 25±2  (n=14) |  | 32±5  (n=40) |  | 1.8 |
| Dusenbery(50) | Look-Locker  (0.15-0.2mmol/kg gadopentetate dimeglumine) | 25±4  (n=27) | 27±8  (n=35) | 0.3 |
| **Acute myocardial infarction** | | **Native T1 (ms)** | | | |  |
| Messroghli(51) | MOLLI 3’3’5 (FA 50°)  Remote myocardium  Infarcted myocardium | (n=15)  982±46(19) |  | (n=24)  1011±66  1197±76 |  | 0.5  3.4 |
| Dall’Armellina(52) | \*shMOLLI  Remote myocardium  Infarcted myocardium |  | (n=10)  1166±60(58) |  | (n=41)  1196±56  1257±97 | 0.5  1.1 |
| **Chronic myocardial infarction** | | **Native T1 (ms)** | | | |  |
| Messroghli(51) | MOLLI 3’3’5 (FA 50°)  Remote myocardium  Infarcted myocardium | 982±46(19) |  | (n=24)  987±34  1060±61 |  | 0.1  1.4 |
| Iles(1) | VAST (FA 25°)  Remote myocardium | 975±62  (n=20) |  | 874±74  (n=25) |  | 1.5 |
| Puntmann(31) | MOLLI 3(2)3(2)5 (FA 50º)  Remote myocardium |  | 1055±22 (n=47) |  | 1145±37 (n=91) | 3.0 |
|  |  | **Postcontrast T1 (ms)** | | | |  |
| Iles(1) | VAST (FA 25°)  (0.2 mmol/kg gadopentetate dimeglumine)  Remote myocardium | 543±32  (n=20) |  | 383±17 (n=25) |  | 6.2 |
|  |  | **ECV (%)** | | | |  |
| Ugander(32)  LGE-  LGE+ | MOLLI 3(3)5 (FA 35°)  (0.15 mmol/kg gadopentetate dimeglumine) | (n=11)  25±3 |  | (n=36)  27±3  51±8 |  | 0.6  4.3 |

**Table 3c-i.6. Outcome studies for all-cause mortality (A) and composite cardiac/heart failure (B) endpoints.** §All comers – symptomatic patients referred to a clinical CMR as a part of routine work-up (i.e. ischemic and non-ischemic cardiomyopathies), in analyses these studies typically excluded hypertrophic cardiomyopathy cardiac amyloidosis, Anderson-Fabry disease, adult congenital heart disease, see Methods of respective studies for detail. §§Composite heart failure endpoints may vary between the studies – see annotations for details. HFpEF – heart failure with preserved EF; DCM – dilated cardiomyopathy; follow up is expressed as average/ interquartile range/standard deviation (SD); b –binary variable; tertile –lower-mid tertile vs. upper tertile; NR- Not reported. Order of studies is by the year of publication. P<0.05 is considered significant: \*-<0.05; \*\*<0.01. ¥ shMOLLI is a MOLLI (5(1)1(1)1 (FA 35°) variant utilizing a conditional reconstruction algorithm.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **A. All-cause mortality** | |  |  |  |  | **Univariate** | **Multivariate** |
|  | **Study type** | **Patient population (n),**  **follow-up (months)** | **Sequence** | **Field Strength**  **(Tesla)** | **Myocardial T1 index** | **HR (95%CI), p-value (**\*-<0.05; \*\*<0.01) | **HR (95%CI), p-value (**\*-<0.05; \*\*<0.01) |
| Wong(53) | Observational, single centre | All-comers§  n=793,  9.6 (6-14.4) | Native: MOLLI 5(3)1 (FA35°),  Postcontrast: MOLLI 4(1)2(1)1 (FA 35°)  (0.2-mmol/kg gadoteridol) | 1.5 | ECV (%) | 1.27 (1.18-1.36)\*\* | 1.18(1.09-1.29)\*\* |
| Banypersad (27) | Observational, single centre | Amyloidosis  n=100,  23 | ¥ shMOLLI  (0.1 mmol/kg gadoterate meglumine) | 1.5 | Native T1b(>1044 ms)  ECVb(>0.45) | 5.39 (1.24-23.4)\*  3.84(1.53-9.61)\*\* |  |
| Schelbert(54) | Observational, single centre | All-comers§  n=1172,  20.4 (12-29) | Native: MOLLI 5(3)2 (FA 35°),  Postcontrast: MOLLI 4(1)2(1)1 (FA 35°)  (0.2-mmol/kg gadoteridol) | 1.5 | ECV (%)  ECVb (>28%) | 1.23(1.15-1.3)\*\*  3.60(2.07-6.26)\*\* | 1.14(1.06-1.27)\*\* |
| Puntmann(55) | Observational multicentre | DCM,  n=637,  22 (19-25) | MOLLI 3(2)3(2)5 (FA 50º) (0.2 mmol/kg of gadobutrol) | 1.5/3.0 | Native T1 (10 ms)  ECV (%) | 1.1(1.06-1.15)\*\*  1.09(1.05-1.14)\*\* | 1.1 (1.07–1.17)\*\* |
|  | | | | | Native T1b(>2SD) | 5.2(2.4–14.6)\*\* | 5.4(2.5–15.2)\*\* |
| Native T1b(tertile) | 9.1(3.8-19.2)\*\* | 10.5(3.8–19.2)\*\* |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **B. Composite Cardiac and Heart Failure Endpoints§§** | | | |  |  |  |  |
| Mascherbauer(9) | Observational, single centre | HFpEF  n=100,  23 (±5) | FLASH-IR  (0.1 mmol/kg of gadobutrol) | 1.5 | Postcontrast T1 (ms) | 0.99 (0.98-0.99)\* |  |
| Schelbert(54) | Observational, single centre | All-comers§  n=1172,  20.4 (12-29) | Native: MOLLI 5(3)1 (FA 35°),  Postcontrast: MOLLI 4(1)2(1)1 (FA 35°)  (0.2-mmol/kg intravenous gadoteridol) | 1.5 | ECV (%)  ECVb (>28%) | 1.3(1.19-1.4)\*\*  5.25(2.57-10.7)\*\* | 1.14(1.06-1.27) |
| Kammerlander (2) | Observational, single centre | All comers§  n=473  13(±9) | MOLLI 5(3)3 (FA 35°) for native acquisition  MOLLI 4(1)3(1)2(FA 35°) for postcontrast acquisition (0.1 mmol/kg of gadobutrol) |  | ECV (%) | 1.11(1.05–1.17)\*\* | 1.09(1.03–1.16)\*\* |
| Puntmann(55) | Observational multicentre | DCM  n=637  22 (19-25) | MOLLI 3(2)3(2)5 (FA 50º)  (0.2 mmol/kg of gadobutrol) | 1.5/3.0 | Native T1 (10 ms)  ECV (per %) | (1.01–1.10)\*\*  1.05 (1.02–1.08)\*\* | 1.07 (1.05–1.1)\*\* |
|  | | | | | Native T1b(>2SD) | 4.7 (2.5 – 8.7)\*\* | 4.8 (2.6–9.1)\*\* |
| Native T1b(tertile) | 4.8 (2.9-8.0)\*\* | 4.7 (2.8–8.0)\*\* |

§§Composite cardiac and heart failure outcomes definitions:

(9) hospitalization for HF or death from cardiovascular causes;

(54)HF hospitalization;

(2)cardiac event (hospitalizations for cardiovascular reasons, cardiac deaths), multivariate analyses were performed for imaging parameters separately; in the combined multivariate analysis, clinical and imaging parameters, age, atrial fibrillation, previous CABG, and RV size were identified as the independent predictors.

(55)(death due to HF and HF hospitalization)

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