Does scar burden predict sudden cardiac death in patients with cardiac resynchronization therapy? - A Systematic Review and Meta-Analysis

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Funding Acknowledgements: Type of funding sources: Public grant(s) – National budget only. Main funding source(s): Project No. RRF-2.3.1-21-2022-00004 (MILAB)

Background: Based on latest guidelines, scar burden assessment may have a crucial role in appropriate device choice in cardiac resynchronization therapy (CRT), but no randomized controlled trials have been made yet.1 Scar burden is associated with a higher prevalence of ventricular arrhythmias (VA) and sudden cardiac death (SCD).2 Late gadolinium enhancement cardiovascular magnetic resonance (LGE-CMR) can accurately evaluate the extent of myocardial scar.3

Purpose: Our aim is to investigate the association between scar burden and SCD risk in cardiac resynchronization therapy patients.

Methods: We performed a systematic literature search on MEDLINE using the PubMed, Embase, Scopus, and CENTRAL databases. Heart failure patients with reduced ejection fraction and CRT therapy were collected. The primary endpoint was sudden cardiac death events. Meta-analyses were performed using the META and DMETAR packages in R, using a random-effects model. The risk of bias was assessed using Quips tool and the quality of evidence was evaluated using the GRADE assessment.

Results: 18 eligible articles have been included in our study, with a total of 2917 patients, of whom 830, 1324, and 391 have been implanted with an ICD, CRT-D, CRT-P respectively. Altogether 59.05 % of the total population were LGE-CMR positive. The average proportion of appropriate ICD shock was 15.65 % per the total population during the median follow-up time of 39.45 months. Based on the univariate analysis of 14 articles, the cumulative hazard ratio of developing sudden cardiac death events, in the scar burden positive population compared to scar burden negative was 1.95 with CI: 1.29-2.96 p<0.001. The multivariate analysis shows the HR of 1.88 with CI: 1.20-2.93 p<0.001. There were 4 articles using the competing risk model which is considered to be the highest evidence level. Based on that analysis we found only a trend with an HR of 1.55 CI: 0.75-2.92. Calculating from the event numbers based on 8 eligible articles, the high scar burden group had 5.55 higher odds of getting SCD events. (OR: 5.55. CI 2.52-12.22 p<0.001).

Conclusion: In our meta-analysis, LGE-CMR was associated with a trend toward appropriate device therapy and can identify a subgroup of patients with an increased risk of life-threatening VA. Based on our results performing an MRI before device implantation might be important to select high-risk patients for SCD.
Forest plot uni. H.R.

### Study

- **Armenta 2012**: Hazard Ratio (HR) = 1.04, 95% CI [1.02; 1.06], Weight = 9.06%
- **Berdibekov 2021**: HR = 1.07, 95% CI [1.03; 1.11], Weight = 9.06%
- **Alexandre 2013**: HR = 1.08, 95% CI [1.04; 1.12], Weight = 9.06%
- **Chen 2014**: HR = 1.15, 95% CI [1.14; 1.16], Weight = 9.06%
- **Acosta 2018**: HR = 1.21, 95% CI [1.10; 1.33], Weight = 9.02%
- **Balaban 2021**: HR = 1.30, 95% CI [0.92; 1.84], Weight = 8.53%
- **Bilchick 2019**: HR = 2.08, 95% CI [1.14; 3.80], Weight = 7.63%
- **Elming 2019**: HR = 2.27, 95% CI [1.17; 4.41], Weight = 7.38%
- **Barison 2019**: HR = 2.42, 95% CI [1.30; 4.51], Weight = 7.55%
- **Piers 2015**: HR = 2.71, 95% CI [1.10; 6.68], Weight = 6.37%
- **Gao 2012**: HR = 3.65, 95% CI [0.49; 27.29], Weight = 2.92%
- **Perazzolo 2014**: HR = 4.17, 95% CI [1.56; 11.17], Weight = 6.02%
- **Sanchez-Somonte 2021**: HR = 10.00, 95% CI [1.34; 74.71], Weight = 2.92%
- **Leyva 2022**: HR = 19.50, 95% CI [6.40; 61.89], Weight = 5.43%

### Random effects model

- **Prediction interval**: 1.95 [1.29; 2.96], Weight = 100.00%

**Heterogeneity**: $I^2 = 92\%$ [88%; 94%], $\chi^2 = 0.50$, $p < 0.001$

**Test for overall effect**: $z = 3.14$ ($p = 0.002$)

- Decreased risk in Scar negative
- Increased risk in Scar positive