Local, non-systemic, and minimally invasive therapies for calcinosis cutis: a systematic review

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**Authors (ORCID iDs)**: Joanna Nowaczyk (0000-0001-7438-3559)\(^a\), Michał Zawistowski (0000-0002-5173-6283)\(^a\), Piotr Fiedor, MD, PhD, Prof.\(^a\)

\(^a\)Department of General and Transplantation Surgery, Medical University of Warsaw, Warsaw, Poland

**Corresponding author**: Piotr Fiedor, MD, PhD, Prof., Department of General and Transplantation Surgery, Medical University of Warsaw, Nowogrodzka 59, 02-006 Warsaw, Poland, email: piotrfiedor@wp.pl
### Table S1. Search queries used to collect the data

| Database            | Search query                                                                 | Filters | Date of last search | Number of records |
|---------------------|------------------------------------------------------------------------------|---------|---------------------|-------------------|
| Pubmed              | ((Calcinosis[MeSH Terms] AND Skin[MeSH Terms]) OR (calci* cutis)) AND ("sodium thiosulfate"[Supplementary Concept] OR Lithotripsy[MeSH Terms] OR "Laser Therapy"[MeSH Terms]) | none    | March 14, 2021      | 153               |
| Embase              | 'skin calcification'/exp AND ('sodium thiosulfate'/exp OR 'extracorporeal shock wave lithotripsy'/exp OR 'laser'/exp) | none    | March 14, 2021      | 128               |
| Web of Science      | ((skin calcification) AND ((sodium thiosulfate) OR (extracorporeal shock wave lithotripsy) OR ESWL OR laser)) | none    | March 14, 2021      | 129               |
| Study | Study design | Q1 | Q2 | Q3 | Q4 | Q5 | Q6 | Q7 | Q8 | Q9 | Q10 | Q11 | Q12 | Q13 | Overall risk |
|-------|--------------|----|----|----|----|----|----|----|----|----|-----|-----|-----|-----|-------------|
| Topical sodium thiosulfate | Abott et al. (2020) | Case report | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ? | ✓ | | | | | Moderate |
| | von Hodenberg et al. (2020) | Case series | ✓ | ✓ | ✓ | ✓ | X | ? | ? | X | ✓ | | | | High |
| | Bhari and Bharti (2019) | Case report | ✓ | ✓ | ✓ | ? | ? | X | X | ✓ | | | | | High |
| | Ma et al. (2019) | Case series | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | | | | Low |
| | Karthik et al. (2019) | Case report | ✓ | ✓ | ✓ | ? | ? | X | X | ✓ | | | | | High |
| | Tajalli et al. (2019) | Case report | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | | | | | Low |
| | Topham et al. (2019) | Case report | ✓ | ✓ | ✓ | ✓ | X | X | ✓ | | | | | | High |
| | García-García et al. (2017) | Case report | ✓ | X | ✓ | ✓ | ? | ✓ | X | ✓ | | | | | Moderate |
| | Jost et al. (2016) | Case series | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | | | | NA |
| | Urreutavizcaya et al. (2016) | Case series | ? | ? | ✓ | ? | ? | ? | ? | ? | ? | ? | ? | NA |
| | Pagnini et al. (2014) | Case report | ✓ | X | ✓ | ✓ | ? | ✓ | X | ✓ | | | | | High |
| | Perez-Moreno et al. (2014) | Case report | ✓ | X | ✓ | ? | ? | ? | ? | ✓ | ✓ | | | | Low |
| | Wolf et al. (2008) | Case report | ✓ | X | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | | | | | Moderate |
| Intraliesional sodium thiosulfate | López-Sundh et al. (2020) | Case report | ? | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | | | | | Low |
| | Olesen and Page (2020) | Case series | ✓ | ✓ | ? | ✓ | X | ? | ? | ✓ | | | | | Moderate |
| | Winter et al. (2020) | Double-blind, placebo-controlled pilot study | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | X | ✓ | ✓ | ✓ | ✓ | ✓ | Low |
| | Tonial et al. (2018) | Case series | ✓ | ✓ | ? | ? | ? | ? | ? | ✓ | ✓ | ✓ | ✓ | | Moderate |
| | Goossens et al. (2017) | Case series | X | ✓ | ✓ | ? | ? | ? | ? | ✓ | ✓ | ✓ | ✓ | NA |
| | Gunasekera et al. (2017) | Case report | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | | | | Moderate |
| | Oh et al. (2017) | Case report | ✓ | X | ✓ | ? | ? | ? | ? | X | X | | | | | Low |
| | Baumgartner-Nielsen and Olesen (2016) | Case series | X | ✓ | ✓ | ? | ✓ | ✓ | ✓ | ? | ✓ | ✓ | | | NA |
| | Smith et al. (2013) | Case report | ✓ | X | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | | Moderate |
| CO₂ laser | Cannarozzo et al. (2020) | Case series | ✓ | ✓ | ? | ? | ? | ? | ? | X | ✓ | ✓ | ✓ | NA |
| | Aristazabal et al. (2019) | Case report | ? | ✓ | ✓ | ✓ | ✓ | ✓ | X | ✓ | | | | | Low |
| | Weig et al. (2019) | Case report | ✓ | X | ✓ | ✓ | ✓ | ✓ | ? | ? | | | | | Moderate |
| | Zarate et al. (2017) | Case report | ✓ | X | ✓ | ✓ | ✓ | ? | ? | ✓ | | | | | Moderate |
| | Kutlubay et al. et al. (2014) | Case report | ✓ | X | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | | | | | Low |
| | Joo et al. (2004) | Case report | ✓ | X | ✓ | ✓ | X | ? | X | ✓ | | | | | Moderate |
| | Chamberlain and Walker (2003) | Case report | ✓ | X | ? | ? | ✓ | ? | ? | ✓ | ✓ | | | | Moderate |
| | Paek et al. (1996) | Case report | ✓ | X | ✓ | ✓ | ✓ | ? | ? | X | | | | | Moderate |

**Table S2.** Risk of bias assessment with the Joanna Briggs Institute Critical Appraisal tools.
| Study                                      | Study Type           | Questions | Yes | No | Unclear | NA | Risk of Bias |
|--------------------------------------------|----------------------|-----------|-----|----|---------|----|--------------|
| Bottomley et al. (1996)                    | Case series          | ✓         | ?   | ?  | ?       | ✓  | NA           | Moderate   |
| Er:YAG laser                               | Case report          | ✓         | x   | x  | x       | ✓  | High         |
| Meissner et al. (2010)                     | Case report          | ✓         | x   | ?  | ?       | ✓  | High         |
| Diode laser                                | Case report          | ✓         | x   | ?  | ?       | ✓  | High         |
| Wollina (2012)                             | Case report          | ✓         | x   | ?  | ?       | ✓  | High         |
| Picosecond + CO₂ laser                     | Case report          | ✓         | x   | ?  | ?       | ✓  | High         |
| Abrouk et al. (2020)                       | Case report          | ✓         | x   | ?  | ?       | ✓  | High         |
| Extracorporeal shock wave lithotripsy      | Case report          | ✓         | ✓   | ✓  | ✓       | ✓  | NA           | Moderate   |
| Delgado-Márquez et al. (2014)              | Case report          | ✓         | x   | ✓  | ✓       | ✓  | High         |
| Sultan-Bichat et al. (2011)                | Case series          | ✓         | ✓   | ?  | ✓       | ✓  | NA           | Moderate   |
| Chan and Li (2005)                         | Case report          | ✓         | x   | ✓  | ✓       | ✓  | High         |
| Sparsa et al. (2005)                       | Case report          | ✓         | x   | ?  | ✓       | ✓  | High         |
| Extracorporeal shock wave lithotripsy      | Case report          | ✓         | x   | ✓  | ✓       | ✓  | NA           | Moderate   |
| Pavlov-Doljanovic et al. (2018)            | Case report          | ✓         | x   | ✓  | ✓       | ✓  | High         |
| Picosecond laser followed by topical sodium thiosulfate | Case series          | ✓         | ?   | ✓  | ?       | ✓  | NA           | Moderate   |
| Eleryan et al. (2019)                      | Case series          | ✓         | ?   | ✓  | ?       | ✓  | NA           | Moderate   |

Abbreviations: Q, question.

Legend: ✓, Yes; x, No; ?, Unclear; NA, not applicable.

Questions based on the JBI risk assessment checklists (see: https://joannabriggs.org/critical-appraisal-tools) for respective study designs.

Overall risk of bias judgement was ranked as low in case >75% of questions were answered “Yes”, high if the prevalence was <50%, and moderate otherwise.