**Supplementary File**: Assessment of validity of the analyzed studies according to the CONSORT checklist [18] (extended table)

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| Section/  Topic | Item number | Neri et al. (2001) | Sakuramoto et al (2007) | Fujimoto et al. (1977) | Douglass et al. (1982) |
| **Title and**  **Abstract** | 1a  1b | Yes  No. No structured summary. | No  Yes | No  No. No structured summary. | No  No. No structured summary. |
| **Introduction**  Background and  objectives | 2a  2b | Yes  Yes | Yes  Yes | Yes  Yes | Yes  Yes |
| **Methods**  Trial design  Participants  Interventions  Outcomes  Sample size  Randomization  Blinding  Statistical methods | 3a  3b  4a  4b  5  6a  6b  7a  7b  8a  8b  9  10  11a  11b  12a  12b | No  Not applicable  Yes  Yes  Yes  Yes  Not applicable  No  No  No. Method not explained.  No. Type not explained.  No. Not done.  No. Not described.  No  Yes  Yes  Not applicable | Yes  Yes  Yes  Yes  Yes  Yes  Not applicable  Yes  Yes  Yes  No. Minimization was used  No  No. Not described.  No  Yes  Yes  Not applicable | No  No. Of the 129 cases, 32 patients were discounted because it was too soon for evaluation.  Yes  No  Yes  Yes  Not applicable  No  Not applicable  No. It is unclear whether or not the study was randomized. No randomization technique is described.  No  No  No. Not described.  No  No  No  No | No  No. A committee reviewed the eligibility and excluded 12 patients. The investigator excluded 11 more patients. A total of 23 randomized patients were excluded from the analysis.  Yes  No.  Yes  Yes  Not applicable  No.  Not applicable  No. The method of randomization is not clearly explained. Patients were stratified and then randomized, a power analysis was not included  No  No  No. Not described.  No  Yes  Yes  No |
| **Results**  Participant flow  Recruitment  Baseline data  Numbers analyzed  Outcomes and estimation  Ancillary analysis  Harms | 13a  13b  14a  14b  15  16  17a  17b  18  19 | No. In Table 1 of the article only evaluable patients are reported. No information about the number of randomized patients is given.  No. Same as 13a.  Yes (previous publication)  No  Yes  No  Yes  Not applicable  Not applicable  No | Yes  Yes  Yes  Yes  Yes  Yes. Main analysis was correctly ITT. Safety analysis was correctly per protocol.  Yes  Yes  Yes  Yes | No.  No  No  No  No. A Table with demographic characteristics of the analyzed patients is missing.  No. ITT analysis was not performed and not enough power was achieved. From the 129 patients included in the intervention group only 97 were analyzed (75%)  No  Yes  No  Yes | No.  No (see point 3b)  Yes  No  Yes  No. ITT analysis was not performed and not enough power was achieved.  Yes  Not applicable  No  Yes |
| **Discussion**  Limitations  Generalisability  Interpretation | 20  21  22 | No  No  Yes | No. Sponsor was involved in design of trial and collection of data  Yes  Yes | No  No  Yes | Yes  No  Yes |
| **Other information**  Registration  Protocol  Funding | 23  24  25 | No  No  No | Yes  No  No | No  No  No | No  No  No |