Original Article | Clinical Studies

Quality of life with minimally invasive repair of pectus excavatum: a systematic review and meta-analysis

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Background: Minimally invasive repair of pectus excavatum (MIRPE) is a popular method for surgical correction of PE, and its impact on quality of life is a growing area of interest. We performed a systematic review and meta-analysis to evaluate the impact of MIRPE on the quality of life of patients.

Methods: This study was registered with PROSPERO under reference number CRD42020222061. A literature search of PubMed, Cochrane Library, EMBASE and Scopus was conducted from the date of inception till November 23, 2020. We included studies which administered one or more questionnaires on patients up to 60 years old, parents or both, to assess the quality of life before and after MIRPE. Studies not written in English, abstracts, articles without primary data, reviews and studies which combined data on PE and other deformities were excluded. Risk of bias was assessed using the Risk of Bias in Non-randomised Studies of Interventions and the Cochrane risk of bias tool. A random-effects meta-analysis was performed to obtain mean differences for key themes of quality of life before and after MIRPE. Responses from the same questionnaires, as well as common themes across different questionnaires, were compared.

Results: Of the 20 studies identified for systematic review, 7 studies that reported the responses of 478 patients were included in the meta-analysis. Patients who underwent MIRPE experienced an increased self-esteem [standardized mean difference (SMD): 1.38, 95% confidence interval (CI): 0.95 to 1.81, P<0.00001] and a smaller degree of chest interference with their social activities (SMD: 0.84, 95% CI: 0.60 to 1.08, P<0.00001). These findings were consistent even after the implanted bar was removed.

Conclusions: MIRPE may be associated with a better quality of life for patients with PE as self-esteem and extent of chest interference with social activities are improved after the procedure. The key limitations of this study are the lack of high-quality evidence due to paucity of randomized trials, and the significant heterogeneity in reported outcomes due to variations in the questionnaires and timepoints of administration.

Keywords: Pectus excavatum (PE); funnel chest; minimally invasive repair of pectus excavatum (MIRPE); quality of life

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Introduction

Pectus excavatum (PE) is a congenital deformity involving sternal depression into the thoracic cavity. The extent of deformity in PE can be extremely varied. In severe cases, a reduction in exercise capacity as evidenced by chest discomfort and dyspnoea on exertion can present as a result of compromised cardiopulmonary function (1-3). Aside from reduced exercise capacity being a strong indication for surgical repair of PE, many will also offer surgery on account of the condition's negative effects on physical appearance, self-esteem and social interaction (4,5).

In general, there are two surgical approaches: open and minimally invasive. Historically, the Ravitch procedure involved a thoracic midline vertical incision, cartilage resection, xiphoid excision and a transverse external sternal osteotomy (6). The Nuss procedure, which is a minimally invasive repair of PE (MIRPE), was reported in 1998 (7). It involved placement of a substernal metal bar via lateral thoracic incisions under thoracoscopic guidance. MIRPE eventually gained popularity as it was shown to result in shorter operative times and decreased blood loss (8,9), although a second short surgery is required to remove the implanted bar (10).

According to the World Health Organization (WHO), quality of life is defined as a "state of complete physical, mental and social well-being" (11). Given that body image is a cornerstone of personal satisfaction and interpersonal communication, it is therefore a major determinant of one's overall well-being and consequently, the quality of life. Although the MIRPE is a well-received procedure, its actual impact on quality of life is difficult to measure. Current evidence on this subject is also scarce. In this study, we aim to test our hypothesis that MIRPE enhances psychosocial well-being in patients, thereby improving their quality of life. The meta-analyses further verified that MIRPE improves important psychosocial aspects of quality of life, such as self-esteem and participation in social activities. We present this article in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) reporting checklist (12) (available at https://atm.amegroups.com/article/view/10.21037/atm-23-1647/rc).

Highlight box

Key findings

- Minimally invasive repair of pectus excavatum (MIRPE) is associated with a better quality of life for patients with pectus excavatum (PE).
- Self-esteem and the extent of chest interference with social activities are improved after MIRPE, and also after eventual bar removal.

What is known and what is new?

- MIRPE is commonly indicated in patients with reduced exercise capacity due to PE. However, its impact on quality of life is difficult to measure.
- Our study found a consistent improvement in the quality of life of patients after MIRPE, based on analyses of responses to PE-specific questionnaires administered in various studies.

What is the implication, and what should change now?

- In view of the evidence supporting the positive impact of MIRPE on quality of life, patients with PE and their parents should be assured of the effectiveness of MIRPE.

Methods

The study protocol was registered with the international prospective register of systematic reviews (PROSPERO) under reference number CRD42020222061. As the study progressed, the protocol was revised to optimize the quality and quantity of studies included, without any change to the primary outcome of the study. In the interest of maintaining scientific integrity, the authors did not retrospectively alter the initial PROSPERO registration. A comprehensive search was conducted independently by two authors (J.S.M. and J.W.T.) in PubMed, Cochrane, EMBASE and Scopus from the date of inception to November 23, 2020. Combinations and permutations of medical subject headings (MeSH), EMBASE (Emtree) terms (funnel chest, surveys and questionnaires, quality of life) and keywords (pectus excavatum, funnel breast, hollow chest, Ravitch, Nuss, MIRPE, minimally invasive repair, quality of life, QOL, HRQOL, health questionnaire, outcomes, survey, esteem, function) were used. The complete search strategy is depicted in Table S1.

Study selection

Eligible study types were cohort studies, case-control studies and randomized controlled trials. Inclusion criteria comprised studies from any surgical teams which administered one or more assessment questionnaires on patients, parents or both, to assess the quality of life before and after MIRPE. Although MIRPE is typically performed in children and young adults, we noted that middle-aged adults have also undergone PE repair. In order not to miss out on any meaningful data on the impact of MIRPE on quality of life, studies reporting on patients of up to 60 years

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old at the time of surgery (defined as the upper age limit for middle-aged adults) were included. In addition, manuscripts not written in English, conference abstracts, articles without any primary data, reviews, studies that reported combined data on PE and other deformities were excluded. References of the selected articles were also reviewed to identify additional relevant studies.

Data extraction and management

Two reviewers (J.S.M. and J.W.T.) independently screened the titles and abstracts of the studies, and performed full text reviews of all included studies. The third reviewer (J.K.C.T.) served as the adjudicator in the event of disagreements. Two reviewers (J.S.M. and J.W.T.) extracted relevant data from each study: authors, year of publication, journal of publication, title, study design, number of patients, gender, age of patients at surgery, name of assessment questionnaire, timepoints of quality of life assessment, response rates of patients or parents who underwent quality of life assessment, and the outcomes of these assessments. Data was collected in a customized Excel file belonging to the authors.

Assessment of risk of bias

The Risk of Bias in Non-Randomized Studies of Interventions (ROBINS-I) was used to evaluate the results of the included non-randomized studies (13). For each domain in the ROBINS-I, an assessment of either a low, moderate, serious or critical risk of bias was made. The Cochrane Risk of Bias assessment tool was used to assess randomized studies (14).

Statistical analyses

Meta-analyses were performed using Review Manager 5.44 (The Cochrane Collaboration, Copenhagen, Denmark). For each assessment questionnaire, values reported as medians were excluded as these results were assumed not to be normally distributed, and thus unsuitable for meta-analysis. Furthermore, not all questionnaires which reported medians provided sufficient information for the mean and standard deviations to be estimated. Finally, the effect of such estimations on the outcome of the meta-analyses was uncertain. A random effects model was used to generate Forest plots. To maximize precision of the analysis, questionnaires that employed different scales in measuring similar domains were evaluated by utilizing the standardized mean difference (SMD). Statistical heterogeneity was assessed by the I^2 statistic, with values of ≤25%, 26–75% and >75% being classified as low, moderate, and high heterogeneity respectively (15). For high heterogeneity (I^2>75%), sensitivity analysis (backward omission step-wise analysis) was conducted by eliminating one study sequentially to examine each individual study's impact on I^2. P values below 0.05 indicated statistical significance.

Results

Results of literature search

The search identified 3,370 articles, of which 2,011 remained after removal of duplicates. Title and abstract screening resulted in 1,904 excluded articles and the full texts of 107 articles were examined. Among these, 71 articles were excluded as they did not report on quality of life. Out of the remaining articles, 16 were excluded due to the following reasons: lack of at least one questionnaire, lack of assessment either before or after MIRPE, quality of life assessment performed on parties other than patients or parents, combined assessment of pectus carinatum and excavatum, conference abstracts, and non-English articles. Twenty studies were eventually included in the systematic review, of which 8 were included in the meta-analysis (*Figure 1*).

Study characteristics

Table 1 shows the characteristics of the 20 included studies (16-35). Eighteen studies were fully prospective while two studies involved a retrospective review of patient records prior to prospective assessment of quality of life. Of the 20 studies, 17 were cohort studies, 2 were case-control studies and 1 was a randomized controlled trial. Fifteen studies were performed in a single institution, whereas the remaining five were multicenter studies. Two studies compared open surgery versus MIRPE, while the other 18 reported only on MIRPE. A total of 2,023 patients underwent MIRPE, and majority were males. Most of the patients underwent surgery as young adults, and only two studies involved patients who were ≥40 years old at the time of surgery. Six studies reported on the number of inserted bars, with a single bar being more common than two bars. The bar(s) was kept *in-situ* for around 3 years in the seven studies that described it.

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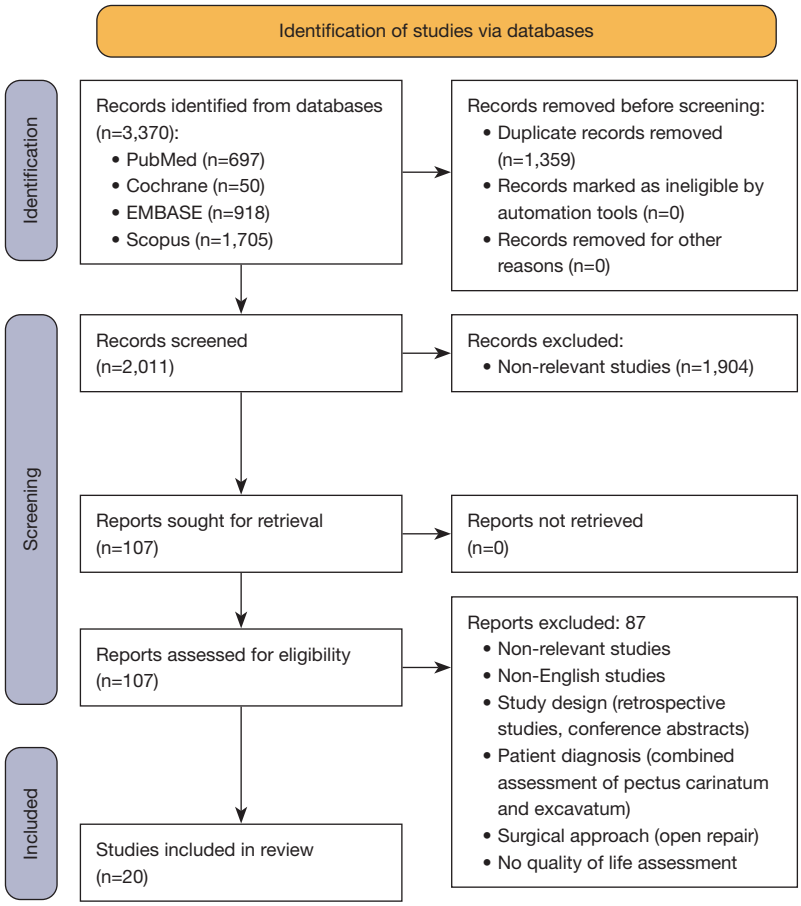

Figure 1 PRISMA flow diagram.

Assessment of the risk of bias

Out of the 19 non-randomized studies, 17 were cohort studies and 2 were case-control studies (*Table 2*). All studies had a low risk of confounding as there was only one intervention received, namely MIRPE. In the selection of participants, five studies were deemed to have a moderate risk of bias as the assessments of quality of life were conducted only after MIRPE. With respect to classification of the intervention and deviations from intended interventions, the risks of bias were low as MIRPE was uniformly performed in all studies. Six studies had a moderate risk of bias due to missing outcome data as the response rate for questionnaires were less than 80%. By nature of their study design, the two case-control studies were assessed to have a moderate risk of bias in the measurement of outcome as the reported quality of life may have been influenced by the researchers' knowledge of whether the patients belonged to the intervention or control group. All 19 studies were deemed to have a low risk of bias in the selection of the reported results as the questionnaires corresponded to the intended assessment of quality of life.

For the single randomized controlled trial, we noted that the randomization was with respect to the stabilizers utilized, and not whether the patients underwent MIRPE. However, as the study design is that of a randomized controlled trial, we used the Cochrane Risk of Bias assessment tool and determined that the study had a low risk of selection, attrition and reporting bias (*Figure 2*). The study had a high risk of performance and detection bias, which we attributed to the difficulty in achieving blinding in trials that involve surgical procedures.

Systematic review of quality of life questionnaires

Of those who underwent MIRPE, a total of 1,623 patients and 727 parents were administered at least one quality of

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Table 1 Characteristics of included studies

Author and year	Design	Country (single or multicenter)	Surgery and number of patients	% (male)	Age at surgery (years)	Number of metal bars inserted	Duration of bar *in-situ*
Lawson 2003 (16)	PCS	USA (multicenter)	MIRPE: 19	NR	8–18	NR	NR
Roberts 2003 (17)	PCS	Canada (single)	MIRPE: 5	NR	NR	NR	NR
Krasopoulos 2006 (18)	PCS	UK (single)	MIRPE: 20	100%	18 [14–37]	1 bar: 19 2 bars: 1	NR
Metzelder 2007† (19)	PCS	Germany (single)	MIRPE: 45	65%	13.5 [6–20]	1 bar: 45 2 bars: 0	31 [23–39] months
Lam 2008 (20)	PCS	Canada (single)	MIRPE: 19; open: 24	88%	15.4±2.2 (MIRPE), 15.1±1.9 (open)	NR	NR
Kelly 2008 (21)	PCS	USA (multicenter)	MIRPE: 283; open: 43	85%	4–21	NR	NR
Jacobsen 2010† (22)	PCC	Denmark (single)	MIRPE: 172	59%	16.4±2.5	NR	NR
Hadolt 2011† (23)	PCS	Austria (single)	MIRPE: 17	76%	15.6±2.5	NR	3 years
Kim 2011† (24)	PCS	Korea (single)	MIRPE: 61	NR	6.8±3.2	NR	2–3 years
Hanna 2013 (25)	PCS	Canada (single)	MIRPE: 73	89%	20 [16–51]	1 bar: 59 2 bars: 14	3 years
Kuru 2015† (26)	PCS	Turkey (single)	MIRPE: 80	85%	16.91±4.37	NR	NR
Kuru 2015 (27)	PCS	Turkey (single)	MIRPE: 88	85.2%	18.44±3.93	NR	NR
Lomholt 2016† (28)	PCC	Denmark (single)	MIRPE: 107	87%	15.3±1.8 (M), 13.2±1.9 (F)	NR	NR
Sacco Casamassima 2016 (29)	PCS	USA (single)	MIRPE: 132	74.5%	30.9 [21.8–55.1]	1 bar: 122 2 bars: 10	32.9±16.9 months
Gibreel 2016 (30)	PCS	USA (single)	MIRPE: 313	79%	15±3	NR	2.4–3.8 years
Luo 2017 (31)	PCS	China (single)	MIRPE: 266	85.7%	19.02±4.42	NR	NR
Zuidema 2018† (32)	PCS	Netherlands (multicenter)	MIRPE: 131	86.2%	16.1±2.3	NR	NR
Zuidema 2019 (33)	PCS	Netherlands (multicenter)	MIRPE: 54	88.8%	17.9 [16–29.4]	NR	3 years
Zuidema 2020† (34)	PCS	Netherlands (multicenter)	MIRPE: 108	87%	16±2.20	1 bar: 99 2 bars: 9	NR
de Carvalho 2021 (35)	RCT	Brazil	MIRPE: 30	90%	17±3.3	1 bar: 27 2 bars: 3	NR

Data has been presented as a range, mean/median [range] or mean ± SD, depending on what was reported in the original study. †, studies included in meta-analyses. PCS, prospective cohort study; MIRPE, minimally invasive repair of pectus excavatum; NR, not reported; PCC, prospective case-control study; RCT, randomized controlled trial; SD, standard deviation.

life assessment. There were twelve different questionnaires identified across the included studies (*Table 3*). However, only three were developed to assess the impact of PE on quality of life, namely the Pectus Excavatum Evaluation Questionnaire (PEEQ), Nuss Questionnaire modified for Adults (NQ-mA) and Single Step Questionnaire (SSQ).

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Table 2 Risk of bias assessment with ROBINS-I for non-randomized studies

Author and year	D1	D2	D3	D4	D5	D6	D7
Lawson 2003 (16)	Low	Low	Low	Low	Low	Low	Low
Roberts 2003 (17)	Low	Low	Low	Low	Low	Low	Low
Krasopoulos 2006 (18)	Low	Low	Low	Low	Low	Low	Low
Metzelder 2007 (19)	Low	Moderate	Low	Low	Low	Low	Low
Lam 2008 (20)	Low	Moderate	Low	Low	Moderate	Low	Low
Kelly 2008 (21)	Low	Low	Low	Low	Low	Low	Low
Jacobsen 2010† (22)	Low	Low	Low	Low	Moderate	Moderate	Low
Hadolt 2011 (23)	Low	Low	Low	Low	Low	Low	Low
Kim 2011 (24)	Low	Low	Low	Low	Moderate	Low	Low
Hanna 2013 (25)	Low	Low	Low	Low	Moderate	Low	Low
Kuru 2015 (26)	Low	Low	Low	Low	Low	Low	Low
Kuru 2015 (27)	Low	Low	Low	Low	Low	Low	Low
Lomholt 2016† (28)	Low	Low	Low	Low	Moderate	Moderate	Low
Sacco Casamassima 2016 (29)	Low	Moderate	Low	Low	Low	Low	Low
Gibreel 2016 (30)	Low	Moderate	Low	Low	Moderate	Low	Low
Luo 2017 (31)	Low	Low	Low	Low	Low	Low	Low
Zuidema 2018 (32)	Low	Low	Low	Low	Low	Low	Low
Zuidema 2019 (33)	Low	Low	Low	Low	Low	Low	Low
Zuidema 2020 (34)	Low	Moderate	Low	Low	Low	Low	Low

D1: bias due to confounding; D2: bias in selection of participants; D3: bias in classification of the intervention; D4: bias due to deviations from intended interventions; D5: bias due to missing outcome data; D6: bias in measurement of outcome; D7: bias in selection of reported result. †, case control studies.

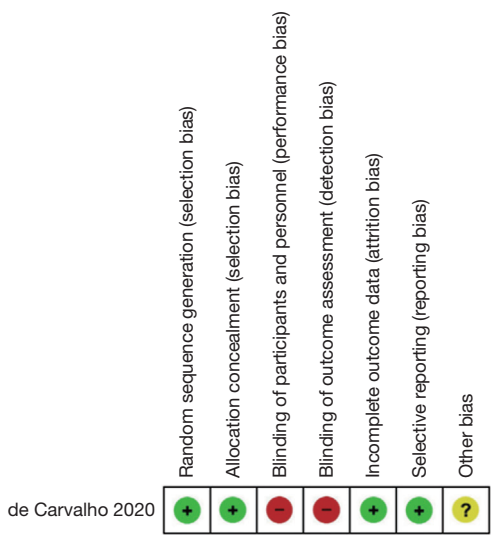

Figure 2 Risk of bias assessment for randomized controlled trial. +, high risk; –, low risk; ?, unclear.

The PEEQ was the pioneer PE-specific questionnaire introduced by Lawson *et al.* (16). It has both child and parent versions and the responses operate on a 4-point Likert scale. All five studies utilizing the PEEQ suggested that MIRPE had a positive impact on psychosocial and physical well-being, of which three studies demonstrated an improvement from preoperative to postoperative scores. Lawson *et al.* (16), Kelly *et al.* (21) and de Carvalho *et al.* (35) included parents in their studies and reported that their concern about the effects of PE on their children diminished post-MIRPE. Krasopoulos *et al.* (18) subsequently modified the PEEQ into the NQ-mA to enable summation of scores, with a higher total score indicating a better quality of life. The NQ-mA was otherwise similar to the PEEQ, with only minor changes to direct questions at adults instead of children. The total scores in the four studies which used the NQ-mA all showed a significant increase postoperatively, suggesting that MIRPE

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Table 3 QoL assessment

Author and year	QoL questionnaire	Number assessed (patients/parents)	Preoperative QoL assessment	Postoperative QoL assessment
Lawson 2003 (16)	PEEQ	19/22	Yes	6–12 months
Roberts 2003 (17)	KSQOL	5/5	No	6–9 months
Krasopoulos 2006 (18)	NQ-mA, SSQ	20/0	Yes	5 months
Metzelder 2007 (19)	SSQ	40/39	No	6 months, 2–3 years
Lam 2008 (20)	PEEQ, CHQ-CF87	23/0 (MIRPE), 11/0 (open)	No	14.1±11.5 months (MIRPE), 15.3±9.2 months (open)
Kelly 2008 (21)	PEEQ	264/291	Yes	12 months
Jacobsen 2010 (22)	CHQ-CF87 (patients only), CHQ-PF50 (parents only), NQ-mA, SSQ	119/119	No	6–30 months
Hadolt 2011 (23)	OEQ, FBCS, SCL-90-R	17/17	Yes	4 years
Kim 2011 (24)	KSQOL	39/39	Yes	5 years
Hanna 2013 (25)	SSQ	51/0	Yes	Exact timepoint NR
Kuru 2015 (26)	NQ-mA	80/80	Yes	6 months
Kuru 2015 (27)	NQ-mA	88/0	Yes	6 months
Lomholt 2016 (28)	CHQ-CF87 (patients only), CHQ-PF50 (parents only)	85/85	Yes	3 months, 6 months
Sacco Casamassima 2016 (29)	SSQ	39/0	No	32.9±16.9 months
Gibreel 2016 (30)	PEEQ	145/0	No	7.1 (0.1–15.7) years
Luo 2017 (31)	SCL-90	266/0	Yes	12 months
Zuidema 2018 (32)	WHO-QOLbref (23 patients), CHQ-CF87 (82 patients), both (26 patients)	131/0	Yes	6 weeks, 6 months
Zuidema 2019 (33)	SF-36	54/0	Yes	12 months
Zuidema 2020 (34)	SSQ	108/0	No	6 weeks, 6 months, 12 months, 24 months
de Carvalho 2021 (35)	PEEQ	30/30	Yes	6 months

QoL, quality of life; PEEQ, Pectus Excavatum Evaluation Questionnaire; KSQOL, Keith-Schalock's Quality Of Life questionnaire; NQ-mA, Nuss Questionnaire modified for Adults; SSQ, Single Step Questionnaire; CHQ-CF87, Child Health Questionnaire-Child Form 87; CHQ-PF50, Child Health Questionnaire-Parent Form 50; OEQ, Operation Expectation Questionnaire; FBCS, Frankfurter Body Concept Scales; SCL-90-R, Symptom Checklist-90-Revised; SCL-90, Symptom Checklist-90; WHO-QOLbref, World Health Organisation Quality of Life; SF-36, 36-item Short Form survey.

had a positive impact on quality of life.

As its name implies, the SSQ provides information on both preoperative and postoperative outcomes despite only a single administration. Krasopoulos *et al.* (18) also opined that the SSQ can be used to assess satisfaction with MIRPE by its overall score. In all six studies with the SSQ, patients had high levels of satisfaction. In addition, there was an improvement in patients' self-esteem and the extent which their chests interfered with social activity. Zuidema *et al.* (34) demonstrated that these improvements were consistent even when the SSQ was administered at four different timepoints post-MIRPE. Although patients experienced at least moderate pain during the hospital stay, Metzelder *et al.* (19), Hanna *et al.* (25) and Sacco Casamassima *et al.* (29) concluded that pain became mild or absent after the metal bar was explanted.

A total of four studies utilized the Child Health Questionnaire-Child Form 87 (CHQ-CF87), of which

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Jacobsen *et al.* (22) and Lomholt *et al.* (28) additionally administered the Child Health Questionnaire-Parent Form 50 (CHQ-PF50) on parents. Both the CF87 and PF50 are generic tools designed to evaluate the physical, emotional, behavioral and social domains of health, with a higher score indicating better well-being. Lomholt *et al.* (28) and Zuidema *et al.* (32) demonstrated that the domain scores increased post-MIRPE and this trend was sustained at 6 months postoperatively. Lam *et al.* (20) showed there was no difference in the CHQ mean scores between MIRPE and open repair, but did not compare scores before and after MIRPE. Similarly, the case-control study by Jacobsen *et al.* (22) showed higher CHQ scores in the MIRPE group but there was no preoperative comparison.

The assessment questionnaire based on Keith-Schalock's Quality of Life (KSQOL) model was used in two studies to assess the following: satisfaction, social belonging, empowerment and well-being. Roberts *et al.* (17) administered the questionnaire on a small group of 5 patients and their parents, both preoperatively and postoperatively, and found improvements in all four domains. In the study by Kim *et al.* (24) which employed a modified version of the questionnaire, similar results were shown. The Symptom Checklist-90 (SCL-90), which evaluates symptoms of mental disorders, was also utilized in 2 other studies. Luo *et al.* (31) showed that symptoms decreased after MIRPE while Hadolt *et al.* (23) only reported that data from the SCL-90 were in the normal range. The World Health Organisation Quality of Life (WHO-QOLbref), Operation Expectation Questionnaire (OEQ), Frankfurter Body Concept Scale (FBCS) and 36-item Short Form survey (SF-36) were each utilized in only one study. In all of these studies, the results suggested that patients who underwent MIRPE experienced an improvement in quality of life.

Despite the diversity of questionnaires, there was consistency in choosing the 6th postoperative month as a suitable timepoint for quality of life assessment. Twelve studies administered the questionnaires at the 6th postoperative month while the rest did so at various time points from the 12th postoperative month. Out of the 20 included studies, only 6 studies did not have a true preoperative questionnaire administration. However, preoperative scores could be inferred if the SSQ was utilized.

Meta-analysis of included studies

The meta-analysis was conducted in two stages: firstly, comparing patient responses for the same questionnaire across multiple studies, and secondly, comparing patient responses to similar themes across different questionnaires. A total of eight studies that utilized five different questionnaires (SSQ, NQ-mA, CHQ-CF87, KSQOL and FBCS) were included in the meta-analysis. The OEQ, SCL-90 and SCL-90-R were excluded as their content were not directly related to quality of life. The PEEQ was also not included as the scoring scale was in an opposite direction to other questionnaires. The reported scores for the SF-36 lacked standard deviation values, and were thus excluded. Of the two studies that utilized the CHQ-PF50, although one reported mean and standard deviation values, the number of parents assessed was unclear, resulting in an unsuitability for meta-analysis of parental scores. We attempted to contact the respective authors to obtain the required data but were unsuccessful.

In the initial stage, only the SSQ and CHQ-CF87 were assessed as the mean and standard deviation scores were available in multiple studies. For the SSQ, "self-esteem" and "extent of interference with social activities" were found suitable for analysis due to the availability of preoperative and postoperative scores. It must be noted that preoperative scores are a part of the SSQ, despite it being administered only once postoperatively. Three studies with a total of 267 patients revealed a statistically significant improvement in self-esteem after MIRPE [mean difference (MD): 2.11, 95% confidence interval (CI): 1.67 to 2.55, P<0.00001] (*Figure 3A,3B*). The I^2 statistic was 78% which represented high statistical heterogeneity. Omission of the outlier study by Metzelder *et al.* (19) resulted in an improved I^2 statistic of 57%, with the improvement in self-esteem still remaining statistically significant (MD: 2.31, 95% CI: 1.95 to 2.66, P<0.00001). An improvement in the extent of interference with social activities was also observed post-MIRPE (MD: 1.33, 95% CI: 0.90 to 1.76, P<0.00001) (*Figure 4A*,*4B*). Similarly, removal of the study by Metzelder *et al.* (19) reduced heterogeneity to a moderate level with an I^2 statistic of 74%. For the CHQ-CF87 questionnaire, two studies with a total of 213 patients provided data on "self-esteem", "emotional limitation" and "general health". A higher self-esteem was observed in patients post-MIRPE (MD: 4.54, 95% CI: 1.21 to 7.87, P=0.007) (*Figure 5*). However, there was no significant difference in emotional limitation (MD: 4.70, 95% CI: –1.86 to 11.27, P=0.16) (*Figure 6*) and general health after MIRPE (MD: 0.23, 95% CI: –2.90 to 3.36, P=0.89) (*Figure 7*). Although I^2 statistic was 86% in the meta-analysis for emotional limitation, sensitivity analysis

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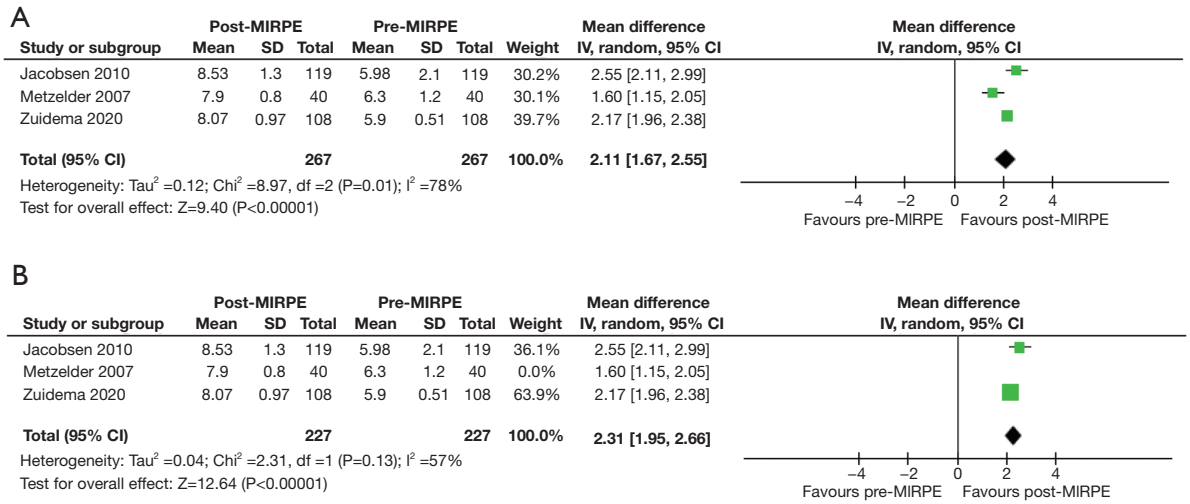

Figure 3 Forest plots comparing self-esteem in the SSQ in patients who underwent MIRPE. (A) Main forest plot. (B) Forest plot with Metzelder 2007 excluded. MIRPE, minimally invasive repair of pectus excavatum; SD, standard deviation; IV, initialization vector; CI, confidence interval; SSQ, Single Step Questionnaire.

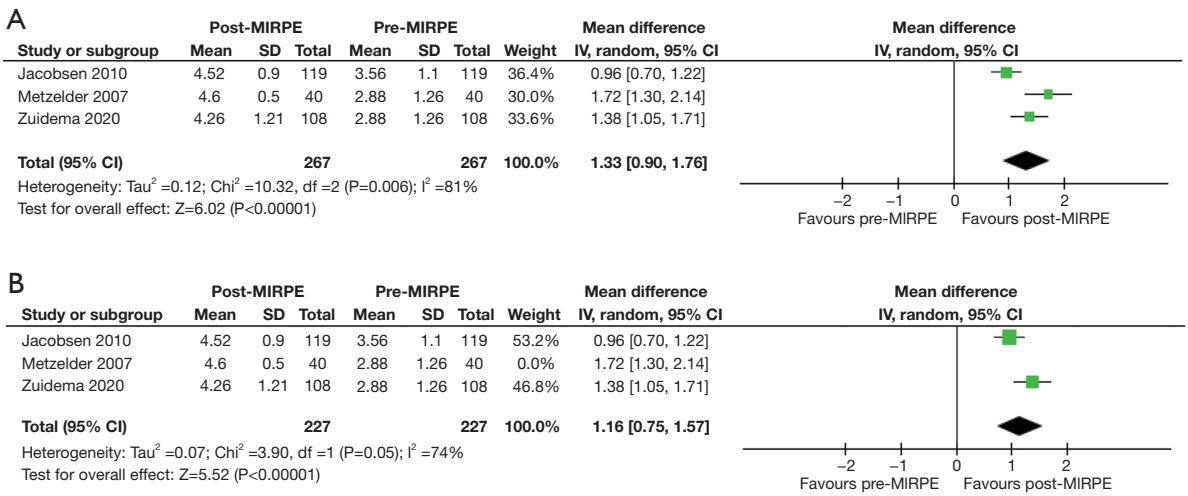

Figure 4 Forest plots comparing extent of interference with social activities in the SSQ in patients who underwent MIRPE. (A) Main forest plot. (B) Forest plot with Metzelder 2007 excluded. MIRPE, minimally invasive repair of pectus excavatum; SD, standard deviation; IV, initialization vector; CI, confidence interval; SSQ, Single Step Questionnaire.

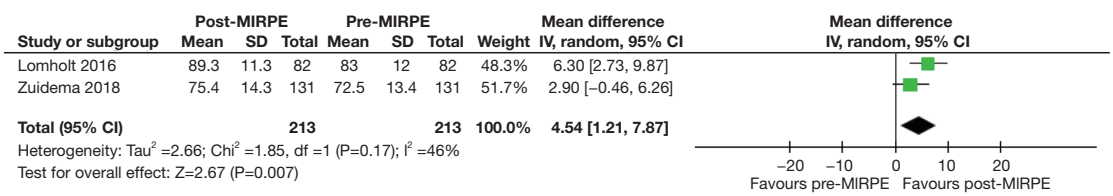

Figure 5 Forest plot comparing self-esteem in the CHQ-CF87 in patients who underwent MIRPE. MIRPE, minimally invasive repair of pectus excavatum; SD, standard deviation; IV, initialization vector; CI, confidence interval; CHQ-CF87, Child Health Questionnaire-Child Form 87.

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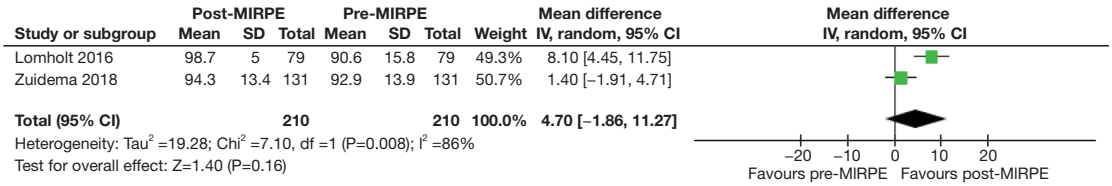

Figure 6 Forest plot comparing emotional limitation in the CHQ-CF87 in patients who underwent MIRPE. MIRPE, minimally invasive repair of pectus excavatum; SD, standard deviation; IV, initialization vector; CI, confidence interval; CHQ-CF87, Child Health Questionnaire-Child Form 87.

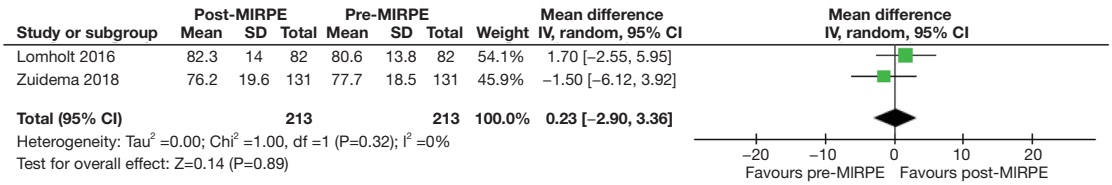

Figure 7 Forest plot comparing general health in the CHQ-CF87 in patients who underwent MIRPE. MIRPE, minimally invasive repair of pectus excavatum; SD, standard deviation; IV, initialization vector; CI, confidence interval; CHQ-CF87, Child Health Questionnaire-Child Form 87.

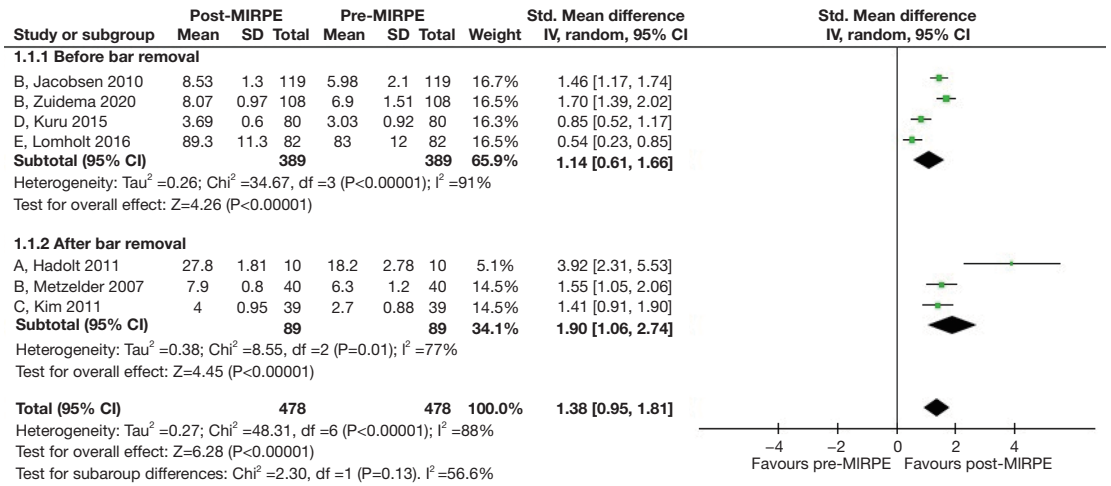

Figure 8 Forest plots comparing self-esteem across all questionnaires in patients who underwent MIRPE. A: self-acceptance of one's body, FBCS; B: self-esteem, SSQ; C: patient's self-confidence, KSQOL; D: feels shy/self-conscious because of chest, NQ-mA; E: self-esteem, CHQ-CF87. MIRPE, minimally invasive repair of pectus excavatum; SD, standard deviation; IV, initialization vector; CI, confidence interval; FBCS, Frankfurter Body Concept Scale; SSQ, Single Step Questionnaire; KSQOL, Keith-Schalock's Quality of Life questionnaire; NQ-mA, Nuss Questionnaire modified for Adults; CHQ-CF87, Child Health Questionnaire-Child Form 87.

was not feasible as there were only two studies included.

We noted that "self-esteem" and "extent of interference with social activities" were two common themes of quality of life across all the included questionnaires. Therefore, in the second stage, responses that fit within these two themes were pooled to perform a random effects meta-analysis. For authors who likely assessed the same patient population across multiple studies, such as Kuru *et al.* (27) and Zuidema *et al.* (34), the most recent study with questionnaire results suitable for meta-analysis was included. Upon analyzing seven studies with a total of 478 patients, we found a statistically significant improvement in self-esteem after

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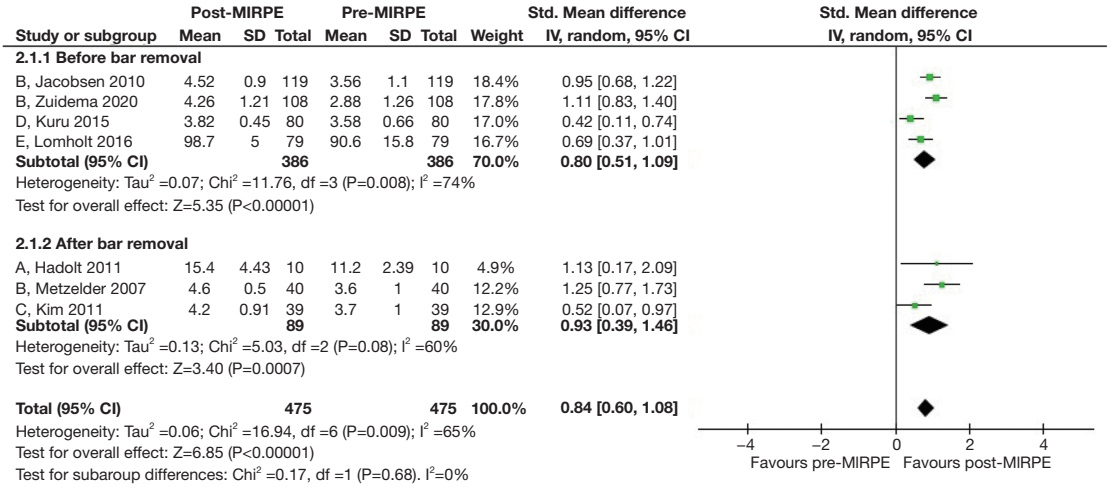

Figure 9 Forest plots comparing extent of interference with social activities across all questionnaires in patients who underwent MIRPE. A: acceptance of one's body by others, FBCS; B: chest interference with social activities, SSQ; C: participation in activities with friends, KSQOL; D: others making fun of him/her because of chest, NQ-mA; E: emotional limitation, CHQ-CF87. MIRPE, minimally invasive repair of pectus excavatum; SD, standard deviation; IV, initialization vector; CI, confidence interval; FBCS, Frankfurter Body Concept Scale; SSQ, Single Step Questionnaire; KSQOL, Keith-Schalock's Quality of Life questionnaire; NQ-mA, Nuss Questionnaire modified for Adults; CHQ-CF87, Child Health Questionnaire-Child Form 87.

MIRPE (SMD: 1.38, 95% CI: 0.95 to 1.81, P<0.00001) and an I^2 statistic of 88% which suggested high heterogeneity (*Figure 8*). To eliminate the presence of the MIRPE bar as a confounder, we segregated the data into before and after bar removal, and repeated the meta-analysis. Based on the results of four studies with a total of 389 patients, self-esteem was still significantly better after MIRPE despite the bar being *in-situ* (SMD: 1.14, 95% CI: 0.61 to 1.66, P<0.0001). Similar findings were observed in the analysis of patients who had the bar removed (SMD: 1.90, 95% CI: 1.06 to 2.74, P<0.00001), with a significant reduction in I^2 to 77%. For the extent of interference with social activities, there was a statistically significant improvement after MIRPE (SMD: 0.84, 95% CI: 0.60 to 1.08, P<0.00001) with an I^2 value of 65% (*Figure 9*). The analysis showed that findings before bar removal (SMD: 0.80, 95% CI: 0.51 to 1.09, P<0.00001) and after bar removal (SMD: 0.93, 95% CI: 0.39 to 1.46, P=0.0007) were similar. It was also observed that statistical heterogeneity was significantly reduced to I^2 of 60% when analyzing the subgroup of studies after bar removal.

Discussion

PE occurs in about 1 out of every 400 individuals (36). Studies have reported that patients with PE suffer from body image dissatisfaction and thus avoid social situations (37-39). To date, there has been a growing number of studies indicating the positive effects of MIRPE on quality of life. Quality of life is a multi-dimensional concept with variable definitions, and psychosocial health has consistently been cited as a key determinant (40-42). However, interpretation of quality of life is often subjective. Therefore, we performed the first systematic review and meta-analysis aimed at summarizing the most pertinent evidence on the impact of MIRPE on quality of life, with emphasis on objective longitudinal effects as measured through questionnaires.

Studies have suggested that the use of disease-specific measures increases the likelihood of showing the effects of pectus correction (43,44). To the best of our knowledge, only three questionnaires specific to PE, the PEEQ, NQ-mA and SSQ, have been published. In particular, the SSQ has high efficiency in longitudinal assessment, given that it splits responses for certain questions into preoperative and postoperative scores. Although the other included questionnaires were not validated specifically for PE, we noted that self-esteem and participation in social activities were psychosocial domains that would encompass most of the content in all questionnaires.

A consistent improvement from preoperative to postoperative scores for self-esteem and extent of chest

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interference with social activities was observed in the present study. The results also showed that patients who underwent MIRPE experienced an overall improvement in quality of life. The positive impact of MIRPE can be explained by its immediate elimination of the pectus deformity. With such a dramatic improvement in physical appearance, it is reasonable to expect self-confidence to improve significantly. This would translate into a reduction in avoidance and concealment behaviors, which would then lead to an increased willingness to engage in social situations (45,46). Ultimately, patients would experience an improved quality of life.

In the assessment of quality of life, pain must also be considered due to its deleterious effects on psychosocial outcomes (47,48). Although it has several advantages over open repair, literature has shown that perioperative pain from MIRPE is comparable to that of the former (49,50). It is therefore remarkable that despite the presence of pain, self-esteem and participation in social activities were all shown to have improved post-MIRPE. The reason why postoperative pain did not translate into a reduced quality of life is likely multifactorial. Based on the present study, it cannot be ruled out that postoperative pain from MIRPE is outweighed by chronic musculoskeletal pain. More studies are therefore needed to fully elucidate the relationship between pain and quality of life in pectus patients who undergo MIRPE. These analyses would be of great relevance, particularly in the era of an increasing emphasis on enhancing recovery after surgery.

From a surgical perspective, the MIRPE is best performed in adolescence when cartilages are malleable (51-53). The adolescent period is also when body image is perceived to be of paramount importance due to its implications on peer acceptance, career building and family planning. However, despite being minimally invasive, MIRPE is still associated with complications such as bar displacement, infection and pneumothorax (54). Therefore, it is imperative to present prospective patients and parents with the physical and psychosocial benefits of MIRPE, aside from cosmesis, in order to justify the conduct of the surgery.

The present study has a few limitations. Firstly, although the included studies were prospectively designed, there was a lack of high-quality evidence due to paucity of randomized controlled trials. It is important to note that the study by de Carvalho *et al.* was only randomized on the type of stabilizers used. Therefore, the included studies are prone to multiple confounders, such as the severity of PE. Additionally, there was significant statistical heterogeneity in the reported outcomes. We posit that this is due to the variability of questionnaires and the timepoints of administration. We attempted to mitigate this by grouping questions under common themes, and performing subgroup analysis stratified by the presence or removal of the implanted bar. The results of the meta-analyses were also subject to selection and responder-recall bias, especially since response rates for the questionnaires were varied. Finally, we propose for future research to focus on the interactions between the psychosocial and physiological outcomes of MIRPE. Although the questionnaires explored physiological outcomes like exercise capacity, comprehensive analysis was not possible due to the lack of relevant data such as pulmonary function tests and echocardiography parameters.

Conclusions

In conclusion, MIRPE is associated with a better quality of life for patients with PE. Furthermore, psychosocial outcomes, specifically self-esteem and extent of chest interference in social activities, are improved after the procedure, and even after eventual bar removal.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-23-1647/rc

Peer Review File: Available at https://atm.amegroups.com/article/view/10.21037/atm-23-1647/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-23-1647/coif). J.K.C.T. serves as an unpaid editorial board member of *Annals of Translational Medicine* from November 2022 to October 2024. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are

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appropriately investigated and resolved.

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Supplementary

Table S1 Complete search strategy

Database	Search terms
PubMed	(funnel chest[MESH] OR funnel chest[tiab] or funnel breast[tiab] OR Ravitch[tiab] OR pectus excav*[tiab] OR hollow chest[tiab] OR nuss[tiab] or MIRPE[tiab] or minimally invasive repair[tiab]) AND (quality of life[MESH] OR QOL[tiab] OR HRQOL[tiab] OR Surveys and Questionnaires[mesh] or quality of life[tiab] or health questionnaire[tiab] or outcomes[tiab] or survey[tiab] or esteem[tiab] or function[tiab])
Cochrane	
#1	MeSH descriptor: [Funnel Chest] explode all trees
#2	("funnel chest" OR "funnel breast" OR Ravitch OR "pectus excavatum" OR "hollow chest" OR nuss OR MIRPE OR "minimally invasive repair"):ti,ab,kw
#3	MeSH descriptor: [Quality of Life] explode all trees
#4	MeSH descriptor: [Surveys and Questionnaires] explode all trees
#5	(QOL OR HRQOL OR "quality of life" OR "health questionnaire" OR outcomes OR survey OR esteem OR function): ti,ab,kw
#6	(#1 OR #2) AND (#3 OR #4 OR #5)
Embase	
#1	funnel chest'/exp
#2	funnel chest':ab,ti OR 'funnel breast':ab,ti OR ravitch:ab,ti OR 'pectus excavatum':ab.ti OR 'hollow chest':ab,ti OR nuss: ab,ti OR mirpe:ab,ti OR 'minimally invasive repair': ab,ti
#3	#1 OR #2
#4	quality of life'/exp OR 'questionnaire'/exp
#5	qol:ti,ab OR hrqol:ti,ab OR "quality of life":ti,ab OR 'health questionnaire': ti,ab OR outcomes:ti,ab OR survey:ti,ab OR esteem:ti,ab OR function:ti,ab
#6	#4 OR #5
#7	#3 AND #6
Scopus	(("funnel chest" OR "funnel breast" OR Ravitch OR "pectus excavatum" OR "hollow chest" OR nuss OR MIRPE OR "minimally invasive repair") AND (QOL OR HRQOL OR "quality of life" OR "health questionnaire" OR outcomes OR survey OR esteem OR function))

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