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Epidural analgesia versus intravenous patient-controlled analgesia following minimally invasive pectus excavatum repair: a systematic review and meta-analysis

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Abstract

Background/Purpose—The minimally invasive pectus excavatum repair (MIPER) is a painful procedure. The ideal approach to postoperative analgesia is debated. We performed a systematic review and meta-analysis to assess the efficacy and safety of epidural analgesia compared to intravenous Patient Controlled Analgesia (PCA) following MIPER.

Methods—We searched MEDLINE (1946–2012) and the Cochrane Library (inception–2012) for randomized controlled trials (RCT) and cohort studies comparing epidural analgesia to PCA for postoperative pain management in children following MIPER. We calculated weighted mean differences (WMD) for numeric pain scores and summarized secondary outcomes qualitatively.

Results—Of 699 studies, 3 RCTs and 3 retrospective cohorts met inclusion criteria. Compared to PCA, mean pain scores were modestly lower with epidural immediately (WMD −1.04, 95% CI −2.11 to 0.03, p = 0.06), 12 hours (WMD −1.12; 95% CI −1.61 to −0.62, p < 0.001), 24 hours (WMD −0.51, 95%CI −1.05 to 0.02, p = 0.06), and 48 hours (WMD −0.85, 95% CI −1.62 to −0.07, p = 0.03) after surgery. We found no statistically significant differences between secondary outcomes.

Conclusions—Epidural analgesia may provide superior pain control but was comparable with PCA for secondary outcomes. Better designed studies are needed. Currently the analgesic technique should be based on patient preference and institutional resources.

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Keywords

Minimally invasive pectus excavatum repair; Nuss; Pain control; Epidural; Analgesia

Pectus excavatum is the most common congenital chest wall deformity, occurring in approximately 1 out of every 1000 live births [1]. The surgical repair of this deformity has seen several adaptations during its evolution: most recently the minimally invasive pectus excavatum repair (MIPER), introduced in 1998 [2]. Reported benefits of MIPER include smaller incisions, decreased blood loss, no need for cartilage resection, and reduced operating times [2]. Despite its classification as "minimally invasive," the immediate reshaping of the chest wall during the procedure results in significant post-operative pain [3]. Pain management after MIPER is a challenge and is the primary factor determining the length of hospital stay [4,5].

Epidural analgesia and Patient Controlled Analgesia (PCA) are both widely employed techniques for postoperative pain management [6]. PCA has the advantage of allowing patients to titrate the level of medication, balancing analgesia against sedation [7]. This less invasive technique has been shown to achieve safe and effective analgesia in children [7]. However, the negative side effects of opioid medications, such as respiratory depression, urinary retention, pruritus, nausea, and vomiting can limit its effectiveness in some children [8]. Epidural analgesia is also established as a safe and effective method for postoperative pain management in children [9]. Studies in adult patients suggest epidural analgesia may provide more complete pain relief while avoiding some of the side effects of intravenous opioid infusion [8]. Epidural analgesia is an invasive procedure and is not free of risks such as infections, nerve damage, drug errors, and cardiac or respiratory arrest [10]. Application of this technique also requires experienced and dedicated pediatric anesthesia staff to place the epidural catheter and continue its management post-operatively [3]. Given that both epidural and patient-controlled analgesia have risks and benefits, there is no consensus in the current literature as to which method offers superior pain management following pectus excavatum repair [4,5,11,12].

We systematically reviewed the current evidence comparing epidural analgesia to PCA following minimally invasive pectus excavatum repair. Using these results, we hope to better inform surgeons, anesthesiologists, patients, and their families as they consider options for pain management following MIPER.

1. Methods

1.1. Review protocol

Prior to conducting our systematic review we created a protocol that outlined our planned approach to the identification and selection of studies. We used the methodology of the Cochrane Handbook for Systematic Reviews of Interventions to identify appropriate studies.

Our pre-specified inclusion criteria were: 1) subjects must be children, adolescents, or young adults (mean age <18 years) undergoing MIPER, 2) one study arm receives epidural analgesia for postoperative pain control, 3) a second study arm receives intravenous PCA

analgesia, 4) the study design is either a randomized controlled trial (RCT) or a cohort study, and 5) authors must report at least one of our pre-specified outcomes of interest.

1.2. Outcome measures

Our primary outcome measure was postoperative numeric pain scores. Pain scores were reported on a numerical scale, 0–10 in all included studies.

In order to investigate the efficacy and safety of the two analgesic methods, we divided our secondary outcomes into benefits and harms. Benefits included 1) overall costs, including costs related to operating room time, length of hospital stay, and adverse events, 2) length of hospital stay, 3) duration of treatment and 4) use of rescue analgesics. Harms included 1) epidural related complications, 2) epidural failure or inability to place an epidural and 3) opioid-related side effects.

1.3. Search methods

1.3.1. Databases, search terms, limits, and special strategies—We searched two electronic databases MEDLINE (1946 through September 2012) and the Cochrane Library (all databases, Inception through October 2012). We used exploded Medical Subject Headings (MeSH) and keywords to generate sets for the following themes: Pediatrics, Post-Operative Pain Control, and Minimally Invasive Pectus Excavatum Repair and then the Boolean operator “AND” to find their intersection. We consulted an experienced reference librarian and used no limits or language restrictions. We conducted a review of the references from each included study and searched for unpublished studies using clinicaltrials.gov and Controlled-Trials.com. Our search strategy is included as Appendix 1.

1.4. Study selection

Two authors independently screened all titles and abstracts from the initial search, only excluding those that were clearly ineligible. The same two reviewers performed a full text review of the remaining studies to assess for final eligibility. Non-English language studies were translated and articles by the same author were specifically reviewed for overlapping study populations to prevent duplicate reporting [13–18]. At each step of eligibility screening, we resolved disagreements by discussion, involving a third author if necessary to reach consensus.

1.5. Assessment of methodological quality

The methodological quality of included studies was assessed using both the Cochrane risk of bias tool and the Newcastle-Ottawa Quality Assessment Scale for Cohort Studies as our review included both randomized trials and cohort studies [19,20]. For the Cochrane risk of bias tool we evaluated studies based on randomization, blinding of outcome assessment, completeness of outcome assessment, and selective reporting. We used the Newcastle-Ottawa scale to assess studies in 8 categories, which considered assessment of exposure, outcome, selection, comparability, and follow-up. The impact of methodological quality on summary estimates was evaluated using sensitivity analysis.

1.6. Analysis

1.6.1. Measure of treatment effect—We summarized the numeric pain score results of the included studies using weighted mean differences (WMD). The WMD is a statistic that measures the absolute difference in mean value between two groups in a clinical trial and uses the standard deviation and sample size to calculate the weight given to each study [19]. When pain scores were not presented in table format, we extrapolated pain scores from graphs [4,5,11,12,17]. For one study that reported medians, we estimated the standard deviation using inter-quartile ranges, employing formulas provided in the Cochrane Handbook [12,19]. When standard deviations were not reported, we used an average of the standard deviations from the studies that had reported standard deviation [4,5,11].

Secondary outcomes were inconsistently measured and reported across studies; therefore, we analyzed these results qualitatively. For each reported secondary outcome, we compared the point estimate for the epidural arm to the point estimate for the PCA arm in each study to determine, which arm, if any, was favored. We then examined across all studies reporting the outcome to determine, qualitatively, if epidural, PCA, or neither was favored. When a measure of statistical significance was provided, we incorporated this in our analysis. We assessed the epidural failure rate by evaluating the overall percent of reported epidural failures as well as individual author's qualitative description of this outcome.

1.6.2. Data synthesis—For our primary outcome, we used RevMan 5 software (Cochrane Information Management System) to pool individual study results, weighted by the inverse variance method, and calculate summary statistics and 95% confidence intervals. Since significant heterogeneity was present, we performed this analysis using a random-effects model, which assumes that the individual studies are estimating effects that are not identical, but follow some distribution [19]. As this model takes heterogeneity between studies into account, it is considered to be a more conservative estimate.

1.6.3. Assessment of heterogeneity—We assessed heterogeneity across studies by using I^2 statistics, where a value greater than or equal to 50% indicates a significant level of heterogeneity, and the calculated test for heterogeneity p value, where significant heterogeneity is indicated by a p value less than 0.10. If significant heterogeneity was present, we evaluated the individual studies in order to identify outliers. When outliers were identified, we evaluated study characteristics for sources of heterogeneity. We performed sensitivity analysis when heterogeneity was present by sequentially excluding individual outliers. If we were unable to achieve homogeneity after study exclusion, we still reported our summary estimate and noted heterogeneity. For qualitative analyses, we assessed for heterogeneity by visually inspecting our summary tables for possible outliers.

1.6.4. Assessment of reporting bias—Using RevMan 5 software, we evaluated for publication bias by creating a funnel plot for our primary outcome measure. The funnel plot displays the effect size for pain scores at different time points versus sample size for each study. Publication bias is considered unlikely if the funnel plot appears symmetric on visual inspection [19].

2. Results

2.1. Description of studies

2.1.1. Results of search—We identified 699 potential studies in Medline and The Cochrane Library. In the two trial registries we identified one completed trial, however, the published article was included in our Medline search results [5]. A review of the references of eligible studies identified one unique study, however it was not included in our analysis, as full text review of the translated article revealed it did not meet inclusion criteria [18]. After duplicates had been removed, we excluded 679 articles by screening the titles and abstracts. We screened the full text of the remaining 20 articles. Six studies met our full inclusion criteria (Fig. 1).

2.1.2. Included studies—The characteristics of the three randomized trials and three retrospective cohort studies included in our review are presented in Table 1. The studies were conducted between 1997 and 2012 and took place in four countries: the Unites States, Austria, Croatia, and Spain. The studies included a total of 403 children with a mean age ranging from 11.1 to 15.8 years. The intervention groups all received continuous epidural infusion and all studies used local anesthetics plus opioid (a single study added clonidine to the epidural mixture). The PCA groups received intravenous infusions of various opioid analgesics.

2.1.3. Methodological quality of included studies—Overall the methodological quality of included studies was moderate (Fig. 2). Because the intervention groups all received an epidural catheter, none of the RCTs employed blinding of participants. However, blinding of the outcome assessment would have been feasible and was not utilized in any of our included studies. The observational studies had a Newcastle-Ottawa Scale score ranging from 7 to 8. The demonstration that the outcome of interest was not present at baseline was inferred for all three studies, because our primary outcome was pain and patients should not have pain prior to surgery. The category most often missed by studies was comparability because no studies adjusted for confounding in their data analysis.

2.2. Primary outcome: Numeric pain scores

Epidural was favored over PCA at all time points. However, there were few statistically significant differences, as seen in Fig. 3. Immediately after surgery (Fig. 3A) the mean pain score was modestly lower among epidural patients compared to PCA patients (WMD −1.04, 95% CI −2.11, 0.03; 4 studies, $p = 0.06$), but the result was not statistically significant. At 12 hours (Fig. 3B) the epidural group had a lower mean pain score and the result was statistically significant (WMD −1.12, 95% CI −1.61, −0.62; 4 studies, $p < 0.001$). Epidural was also favored at 24 hours postoperatively (Fig. 3C), but the result was not statistically significant (WMD −0.51, 95%CI −1.05, 0.02; 6 studies, $p = 0.06$). At 48 hours (Fig. 3D) the result also favored epidural and was statistically significant (WMD −0.85, 95% CI −1.62, −0.07; 6 studies, $p = 0.03$). At 72 hours (Fig. 3E) there was no difference in mean pain score between analgesic modalities (WMD −0.16, 95%CI −0.93, 0.61; 4 studies, $p = 0.68$). Of note there was significant heterogeneity in the summary estimates immediately, 48 hours,

and 72 hours after surgery. Publication bias was unlikely, given symmetry on visual inspection of the funnel plot (Fig. 4).

2.3. Primary outcome: sensitivity analysis

2.3.1. Restricted to only RCTs—Given the inherent biases of retrospective cohort studies, we performed a sensitivity analysis restricted to only RCTs (Fig. 5). We found that there was little effect on our summary estimates, except the summary estimate at 24 hours became statistically significant and less heterogeneous (WMD −0.82, 95%CI − 1.35, −0.30, I^2 0%, p = 0.002).

2.3.2. Methodological quality—Sensitivity analysis was also performed by each element of our two methodological quality assessment tools, however this did not result in significant changes in our summary estimates or heterogeneity between studies.

2.4. Secondary outcomes

2.4.1. Benefits: cost, length of stay, operating time, duration of treatment, and rescue analgesics—There was insufficient data for costs, duration of treatment, or rescue analgesics to summarize results across studies. Differences in length of stay (LOS) and operating room (OR) time were neither clinically relevant nor statistically significant except for one study that found LOS was reduced by 15 hours with PCA and one study that found OR time was reduced by 23 minutes with PCA (Table 2) [4,5].

2.4.2. Harms: treatment side effects, epidural complications, and epidural failure—Among studies reporting medication side effects, there were no statistically significant differences in nausea (5 studies), pruritus (3 studies), sedation (4 studies) or respiratory depression (5 studies). In studies reporting on nausea four reported less nausea in the epidural group. Similarly, two studies reported less respiratory depression in the epidural group. The results were comparable across treatment modalities for pruritus and sedation. There were no serious adverse side effects or major epidural complications reported in any of the studies. Three studies reported minor epidural complications, including leak, pain at catheter site, and need for replacement of catheter [12,17,21]. The epidural failure rate, defined as failure to place an epidural or a non-functional catheter, ranged from 0% to 35% (Table 3) [4,5,12,17,21].

2.4.3. Heterogeneity—Our results for the numeric pain scores were heterogeneous at three time points (immediately post-op, 48 hours, 72 hours). While one study appeared to be the outlier for these three time points, removal of this study did not resolve the heterogeneity in our models [21].

In our qualitative analysis of benefits, outliers were seen for both length of stay and operating room time. The study by Weber et al. had substantially longer length of stay compared to the other studies, which may be related to the health care system in Austria [12]. For operating room time, we identified an outlier favoring epidural by over one hour whereas all other studies generally favored PCA. We reviewed the outlying study and found inconsistencies between the text and tables reporting this result [21]. Finally, we also noted

that two studies by a single group had significantly higher epidural failure rates compared to the other studies (22–35% vs 0%) [4,5].

3. Discussion

3.1. Summary of main results

Clinicians have debated whether epidural analgesia or PCA is the preferred method of pain management after MIPER. The results of our review of the current literature suggest that the two methods are comparable in terms of efficacy and safety. Our summary estimates for mean postoperative pain scores favor epidural for the first 48 hours after surgery; however the only statistically significant results were at 12 and 48 hours after surgery. For the remaining time points, there was either a lack of statistical significance or considerable heterogeneity across treatment modalities. When differences were observed, mean pain scores varied between 0.5 and 1 point on the numeric pain scale, which is unlikely to represent a clinically significant difference. Based on our meta-analysis of available evidence, epidural and PCA appear to provide equivalent pain control following MIPER.

When comparing the safety of the two techniques, we evaluated both the benefits and harms. We were unable to make quantitative comparisons given the varied methods of reporting for the various side effects. In a qualitative analysis, we found neither clinically important nor statistically significant differences between treatment arms. There were no statistically significant differences in length of stay or operating room time. Overall, opioid side effects occurred infrequently, with nausea being the most commonly reported. In the five studies that reported on nausea, the epidural patients appeared to experience nausea less frequently overall, however these results were not statistically significant. Neither analgesic technique was associated with any significant adverse events among subjects such as infection, neurologic injury, or respiratory or cardiac arrest. There was a striking variation in the epidural failure rate across studies, reported from 0% to as high as 35%.

3.2. Quality and applicability of the evidence

The methodological quality of the included studies was marginal at best. Given the nature of the analgesic interventions, there was no blinding of subjects or investigators possible with regard to treatment arm, which could potentially introduce performance and assessment bias. However, we feel it is unlikely that patients are biased based on which analgesic technique they receive. Similarly, the assessment of pain scores is based on what patients report and unless assessors inconsistently recorded data, the lack of blinding should not impact our primary outcome measure.

Considering bias within our included studies, selection bias was an area of concern. Of the randomized controlled trials, the randomization procedures were unclear. Further, among the retrospective cohort studies, the method for selection of cases for the treatment groups was not clearly defined.

Two studies from a single institution were included in our review and provided the majority of the patients, thus contributing more weight to our summary estimates. The epidural failure rate at this institution was significantly higher than that reported in the other included

studies (22–35% compared to 0%) and when compared to the pediatric scoliosis literature (0–5%) [4–6,12,17,21–24]. In the RCT from this group 22% of epidural patients crossed over to the PCA group. Therefore, their intent-to-treat analysis may underestimate any efficacy benefit of epidural. In their retrospective cohort study, there was a 35% epidural failure rate and the authors analyzed these individuals separately from the successful epidurals. As the majority of these failures were recognized before the patient left the operating room, we included only the successful epidural group in our meta-analysis. Of note, in the remaining retrospective cohort studies, the selection of cases is not well described, which could potentially underestimate the epidural failure rate in these studies.

Within our review, a dedicated pediatric anesthesia team with expertise in epidural placement and management was discussed in some studies and this may have been an important factor for successful utilization of the epidural technique. Similarly, superior epidural success rates were seen in studies that used imaging confirmation compared to conventional methods, with the former technique supported by a recent report in the pediatric anesthesia literature [17,21,25].

Another important consideration is the age of the patient, as preadolescent children have a more flexible chest wall and may experience less pain than adolescent patients who are closer to skeletal maturity. In the RCT by St. Peter et al., the epidural group was older on average than the PCA group, which may further bias their results [5]. We suggest study protocols include age categories or authors provide a subgroup analysis based on age.

3.3. Potential biases of our review

Given the paucity of RCTs meeting our inclusion criteria, we included retrospective cohort studies. This increases the baseline potential for confounding and measurement bias, which must be carefully considered and adjusted for in the analysis. However, a sensitivity analysis restricted to only RCTs did not change our results significantly. Our database search was limited to Medline and The Cochrane Library, which may subject this review to publication bias, even though a funnel plot of our meta-analysis did not reflect publication bias.

Our primary outcome of numeric pain scores was limited by certain mechanical methods. There was significant variation among studies in the timing and reporting of postoperative pain scores. Therefore, for some time points, not all studies were included in our summary estimate and assumptions were made to combine studies, for example considering 24 hours and postoperative day 1 equivalent. Five of the six studies reported numeric pain scores graphically, requiring data extrapolation from study figures, which may limit our results due to human error. However, data extrapolation from figures is a well accepted method in systematic reviews and has been utilized in similar reviews [26,27]. Further, less than half of included studies reported standard deviations or p-values for their pain score data.

3.4. Agreements and disagreements with other studies or reviews

Our results are supported by other reviews comparing epidural to intravenous opioid analgesia in adult surgery and pediatric scoliosis repair [26,27]. Both populations had better pain control with epidural analgesia, in agreement with our results. The magnitude of benefit was lower in our review compared to these other reviews, which may reflect the

methodological quality of our included studies. In children undergoing scoliosis surgery, nausea was also reduced in the epidural group, which agrees with our qualitative analysis [27].

4. Conclusions

Given the available evidence, we found no clear differences between the two analgesic techniques following minimally invasive pectus excavatum repair, as epidural analgesia and PCA resulted in comparable safety and efficacy outcomes. Although Epidural analgesia may provide superior pain control following MIPER, especially during the early post-operative period, the differences were not clinically relevant. Given our results and the methodological flaws of the included studies, clinical equipoise remains when comparing these two analgesic techniques. We suggest that clinicians and patients select the most appropriate technique on an individual level, based on patient preference and institutional resources.

We feel that a study comparing the use of epidural to PCA must have a dedicated pediatric anesthesia team with sufficient expertise and demonstrated success with the use of epidural analgesia. The epidural failure rate in some of the included studies is unacceptably high and may not represent optimal use of this technique. Many of the studies utilize a T6–T8 epidural, but in our experience, better results are achieved with a T4–T6 epidural to provide complete coverage of the operative field. Finally, we recommend the use of an epidurogram to confirm correct placement, rule out incorrect anatomic location, and predict analgesic coverage [25]. With regards to operative time and cost, the epidural does not need to be placed in the operating room and can be placed in an induction and regional anesthesia area when available.

Beyond better application of analgesic technique, this field of research could benefit from consistency in the definition and measurement of outcomes. To facilitate comparison between studies of postoperative pain, pediatric surgery and anesthesia investigators should agree on a set of standard times to measure pain scores and consistently report means with standard deviations. Due to inconsistencies between studies, we could not make statistical comparisons for many important side effects that impact patient satisfaction and well-being. Therefore, the method for reporting side effects should be uniform across studies.

In our effort to improve trials in pediatric surgery, we should look to the CONSORT guidelines, which have been adopted by the Journal of Pediatric Surgery [28,29]. Our field will benefit if investigators consistently use the same endpoints, measuring the outcomes that are most relevant to our patients. A well-designed randomized controlled trial is still required to objectively answer this unresolved clinical question.

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Appendix 1. Search Strategies

Database(s): Complete Ovid MEDLINE(R)

Dates covered: 1946 through September 2012

Last accessed: 09/26/2012

Search Strategy:

#	Searches	Results
1	exp Pediatrics/	40649
2	exp Child/	1462722
3	exp Infant/	890748
4	exp Adolescent/	1501775
5	exp Young Adult/	247261
6	pediatric$.mp.	192377
7	adolescent$.mp.	1525123
8	Child.mp.	1583422
9	infant$.mp.	974333
10	Children.mp.	677130
11	childhood.mp.	150370
12	young adult$.mp.	290901
13	or/1–12	3085716
14	exp Analgesia, Epidural/	6466
15	exp Anesthesia, Epidural/	11368
16	exp Anesthesia/	152469
17	exp Analgesia/	30200
18	exp "Anesthesia and Analgesia"/	187040
19	exp Analgesia, Patient-Controlled/	3387
20	exp Pain Management/	14626
21	exp Pain, Postoperative/	26028
22	Epidural anesthesia.mp.	4712
23	Epidural analgesia.mp.	5212
24	Patient-controlled analgesia.mp.	2901
25	postoperative pain management.mp.	1040
26	postoperative pain control.mp.	795
27	exp Pain Measurement/	53971
28	thoracic epidural analgesia.mp.	454
29	or/14–28	256564
30	exp Funnel Chest/	1538
31	pectus excavatum.mp.	1262
32	funnel chest.mp.	1747
33	Nuss.mp.	278

#	Searches	Results
34	exp Thoracic Surgery/	10029
35	exp Thoracoscopy/	8975
36	exp sternum/	7600
37	thoracoscopy.mp.	7054
38	thoracic surgery.mp.	20140
39	or/30–38	34897
40	13 and 29 and 39	451

Database: The Cochrane Library (all databases)

Dates covered: Inception through October 2012

Last accessed: 10/15/2012

ID	Search	# of results
#1	MeSH descriptor: [Pediatrics] explode all trees	452
#2	pediatrics	13535
#3	pediatric	20778
#4	MeSH descriptor: [Child] explode all trees	1
#5	child	76041
#6	children	76041
#7	childhood	7340
#8	MeSH descriptor: [Infant] explode all trees	11668
#9	infant$	31620
#10	MeSH descriptor: [Adolescent] explode all trees	68652
#11	adolescent$	80245
#12	MeSH descriptor: [Young Adult] explode all trees	6
#13	young adult$	29669
#14	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13	156239
#15	MeSH descriptor: [Analgesia, Epidural] explode all trees	1666
#16	epidural analgesia	4525
#17	MeSH descriptor: [Anesthesia, Epidural] explode all trees	1698
#18	epidural anesthesia	5069
#19	thoracic epidural analgesia	583
#20	MeSH descriptor: [Analgesia, Patient-Controlled] explode all trees	1484
#21	patient-controlled analgesia	2786
#22	MeSH descriptor: [Anesthesia] explode all trees	14304
#23	MeSH descriptor: [Analgesia] explode all trees	5570
#24	MeSH descriptor: [Anesthesia and Analgesia] explode all trees	20191
#25	MeSH descriptor: [Pain Management] explode all trees	1077

ID	Search	# of results
#26	MeSH descriptor: [Pain Measurement] explode all trees	12911
#27	MeSH descriptor: [Pain, Postoperative] explode all trees	8634
#28	postoperative pain control	15643
#29	postoperative pain management	2450
#30	#15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29	40318
#31	MeSH descriptor: [Funnel Chest] explode all trees	15
#32	funnel chest	727
#33	MeSH descriptor: [Thoracic Surgery] explode all trees	155
#34	thoracic surgery	5261
#35	MeSH descriptor: [Thoracoscopy] explode all trees	222
#36	thoracoscopy	186
#37	MeSH descriptor: [Sternum] explode all trees	172
#38	pectus excavatum	13
#39	nuss	35
#40	#31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39	6090
#41	#14 and #30 and #40	246

Database: ClinicalTrials.gov

Dates covered: 2000 through October 2012

Last accessed: 10/17/12

The electronic database ClinicalTrials.gov was searched on October 17th, 2012 beginning with the broad search terms “pectus excavatum OR funnel chest”. This search resulted in 9 studies, however only a single completed study was related to post-operative pain, “Pain Management for pectus excavatum Repair” (The published results of this study are already included by our Medline search strategy). An additional targeted search was performed using “pectus excavatum” as Conditions and “epidural analgesia OR Patient-Controlled Analgesia” as Interventions. This search resulted in one completed trial, which was the same trial noted above.

Database: Controlled-Trials.com

Dates covered: 1998 through October 2012

Last accessed: 10/17/12

The electronic database Controlled-Trials.com was searched on October 17th, 2012 using “pectus excavatum OR funnel chest AND analgesia” as a search terms (changing “analgesia” to “epidural” or “PCA” gave the same search results). The search resulted in 6 total trials, although the only relevant trial was the same completed trial that we identified with ClinicalTrails.gov.

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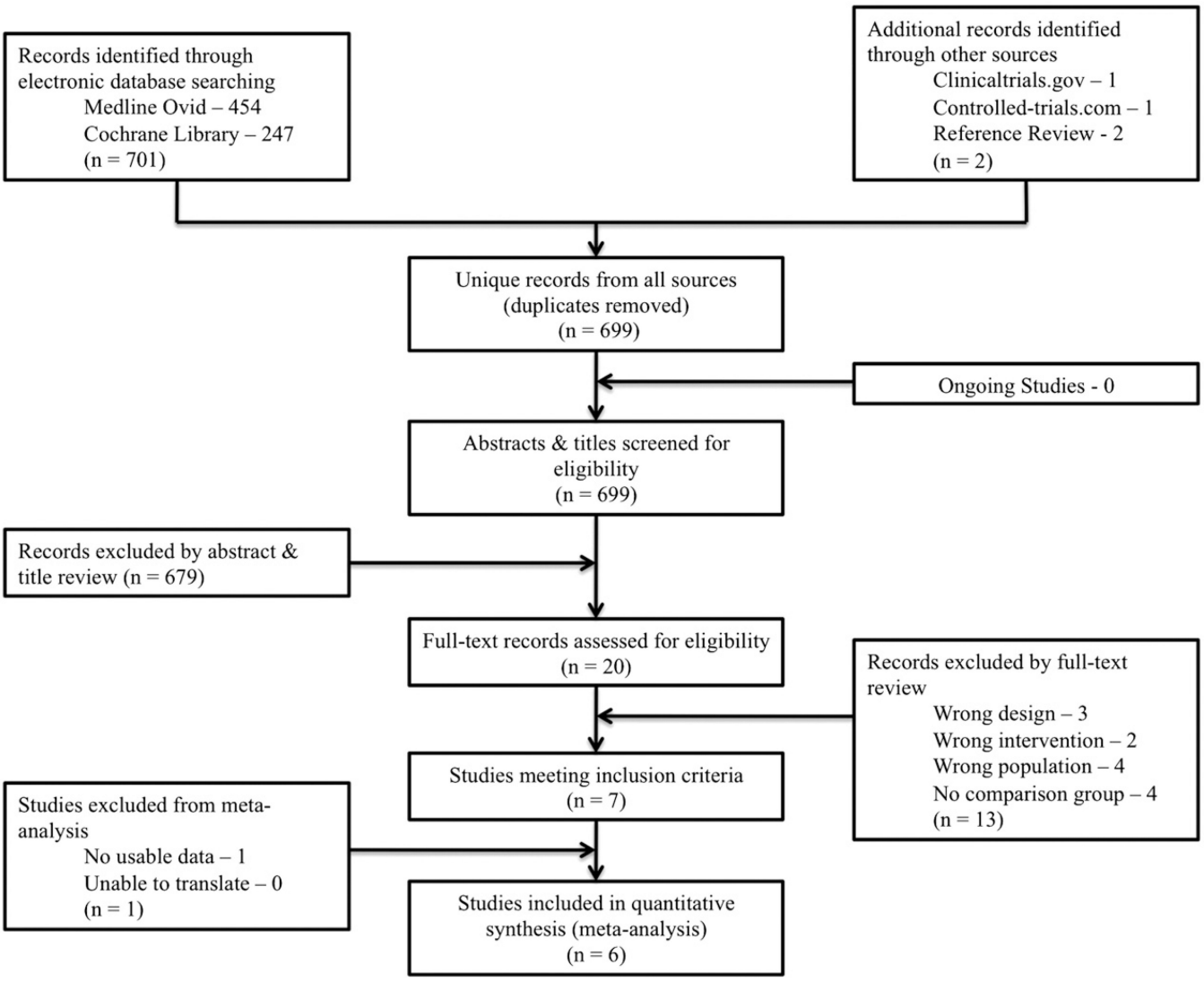

Fig. 1.
PRISMA flow diagram for collection and appraisal of potential studies.

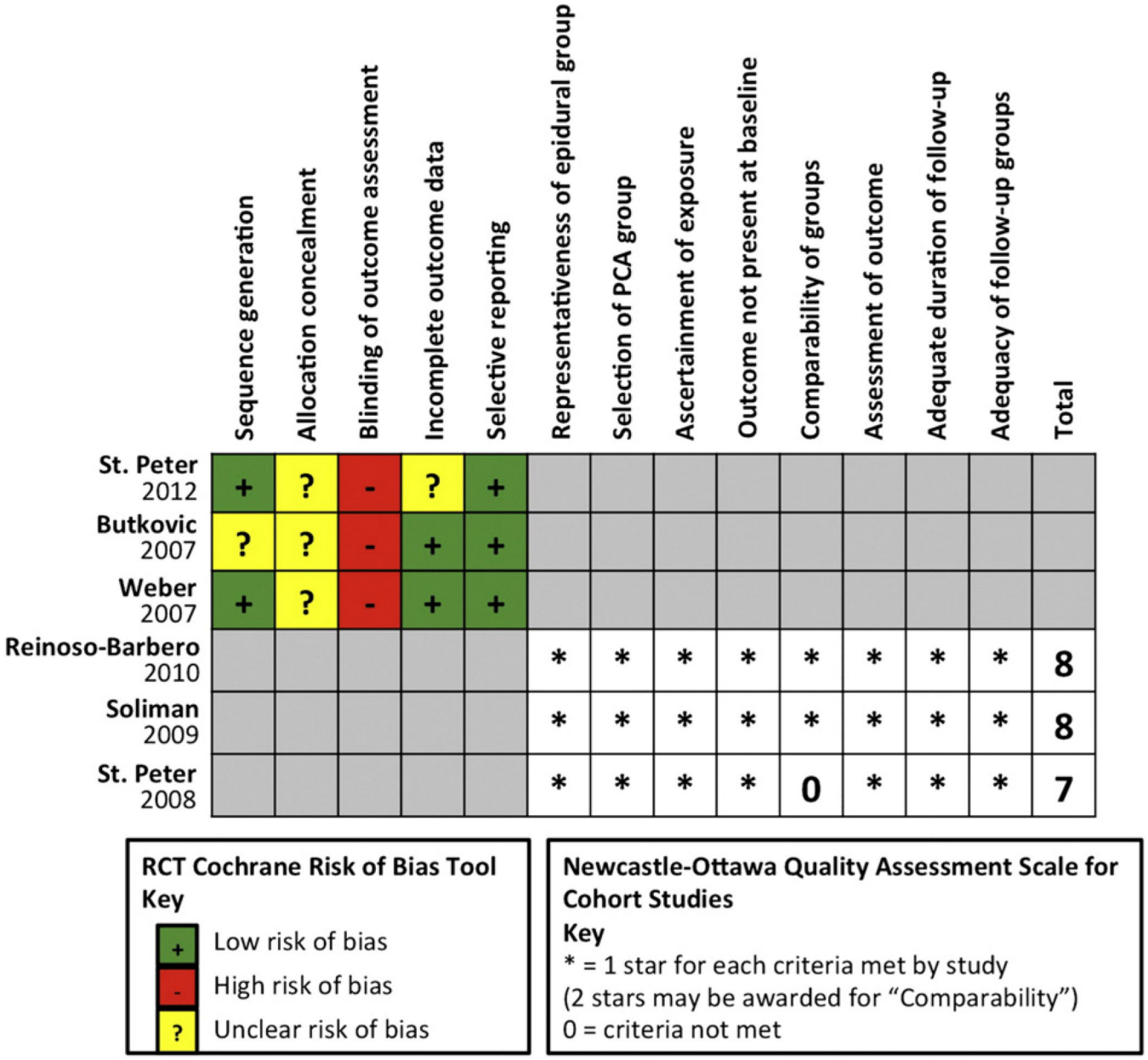

Fig. 2.

Assessment of methodological quality of included studies based on Cochrane Risk of Bias Tool for randomized control trials (RCT) or the Newcastle-Ottawa Quality Assessment Scale for cohort studies.

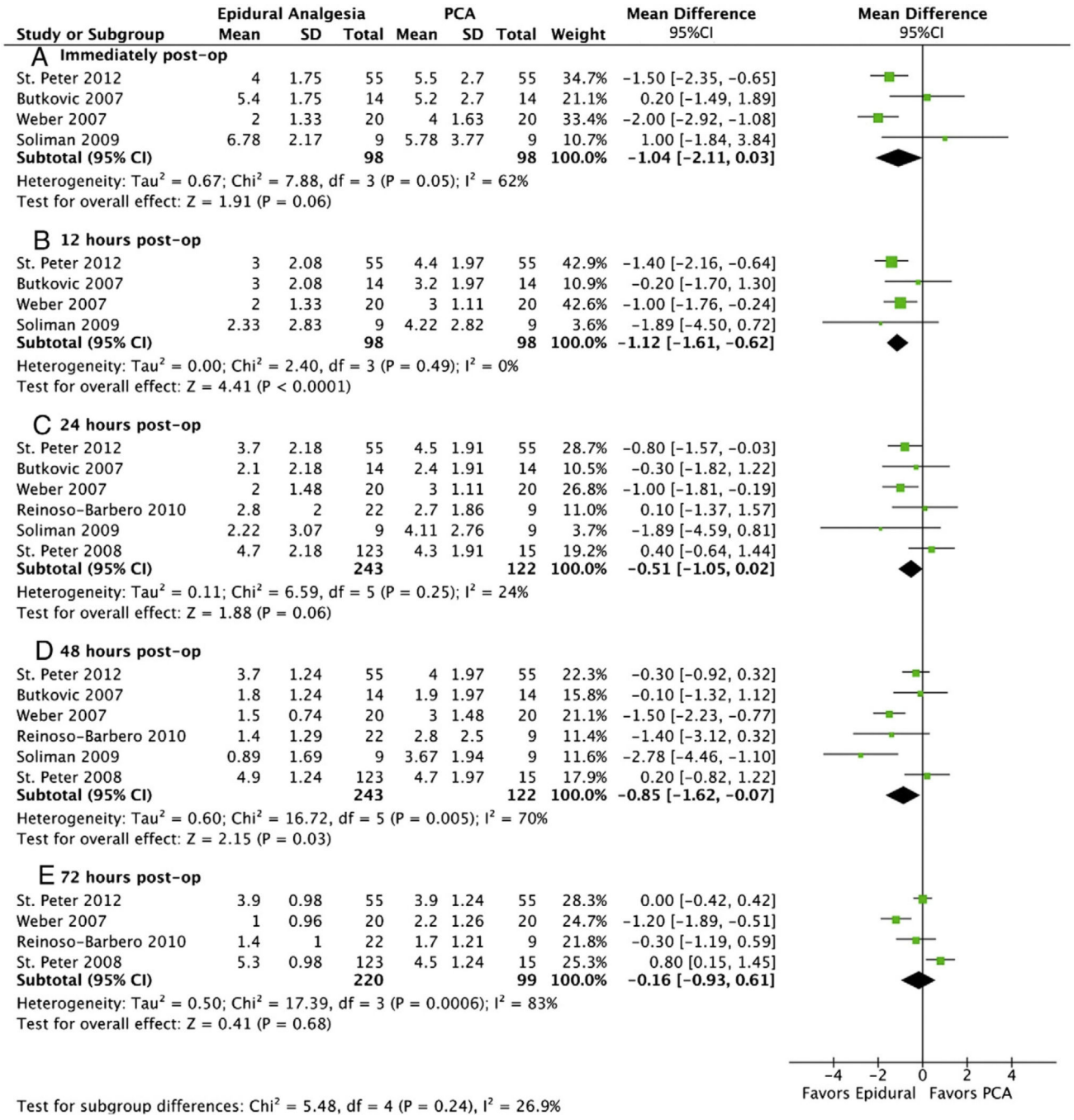

Fig. 3.

Forest plot of primary outcome data (pain scores on a 0–10 numeric scale) for 5 time points after surgery. (Key: PCA = Patient controlled analgesia, SD = standard deviation, 95%CI = 95% confidence interval).

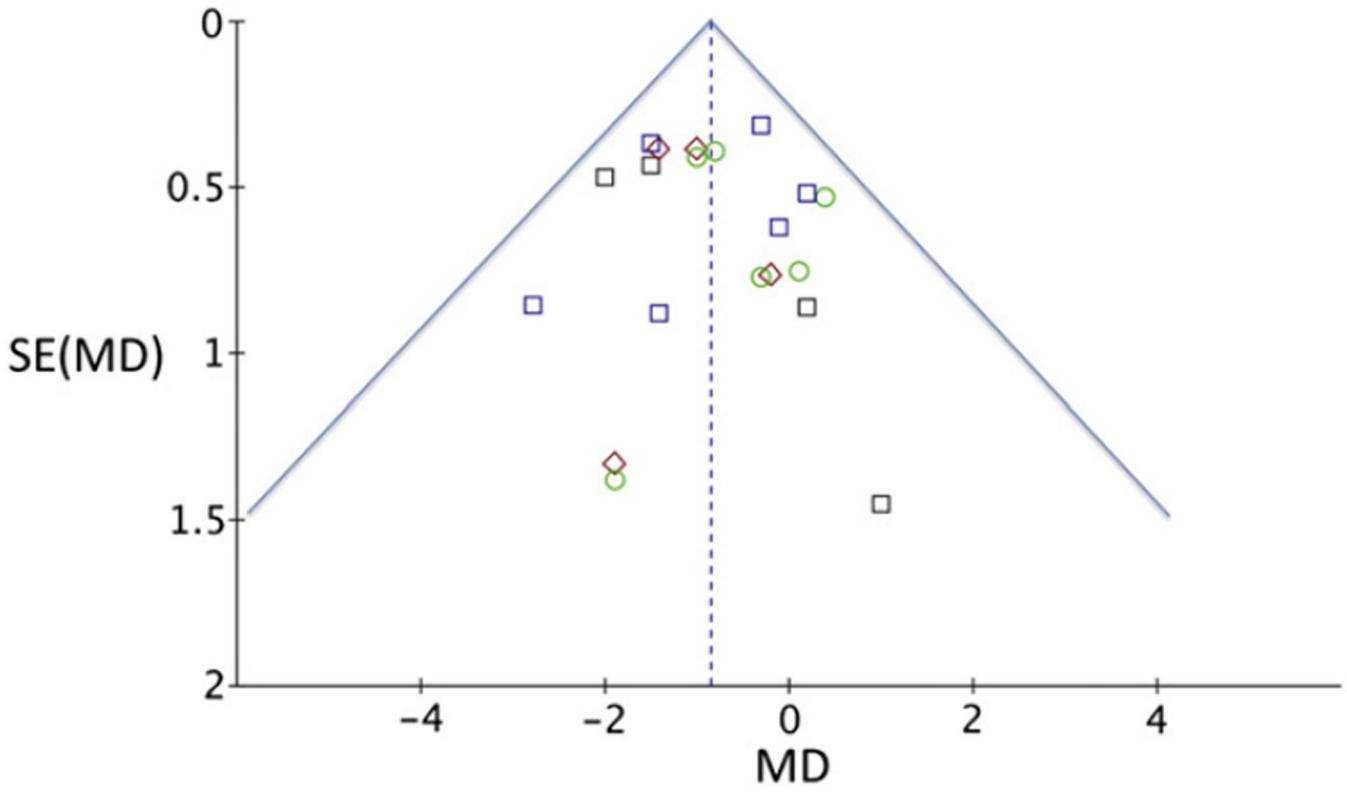

Fig. 4.

Funnel plot assessing publication bias based on reporting of the primary outcome. (Key: SE = standard error, MD = mean difference).

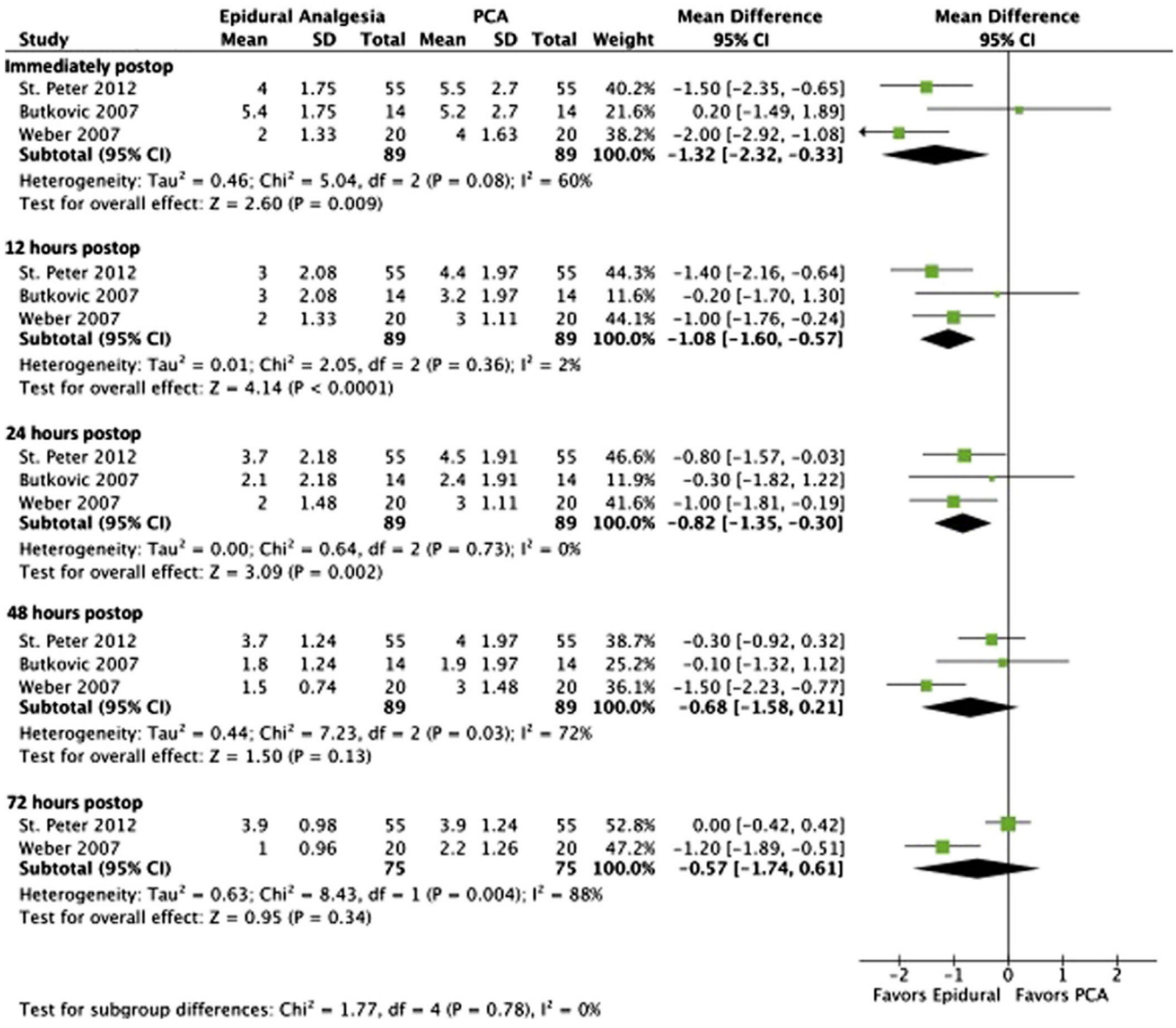

Fig. 5.

Forest plot of primary outcome data (pain scores on a 0–10 numeric scale) for 5 time points after surgery, restricted to only randomized controlled trials. (Key: PCA = Patient controlled analgesia, SD = standard deviation, 95%CI = 95% confidence interval).

Table 1

Characteristics of included studies.

First author, year	Study design	Patients (n)	Mean age (years)	Gender (% male)	Epidural analgesia	PCA	Follow up duration
St. Peter, 2012	RCT	110	15.5	Not reported	Ropivacaine, fentanyl, clonidine	Hydromorphone	Hospital course
Butkovic, 2007	RCT	28	14.5	75%	Bupivacaine, fentanyl	Morphine	6 months
Weber 2007	RCT	40	15.8	80%	Ropivacaine, fentanyl	Morphine	Hospital course
Reinoso-Barbero, 2010	Retrospective cohort	31	11.1	77%	Bupivacaine, fentanyl	Fentanyl	Hospital course
Soliman, 2009	Retrospective cohort	18	14.8	72%	Bupivacaine, hydromorphone	Morphine	Hospital course
St. Peter, 2008	Retrospective cohort	203	13.9	81%	Not reported	Not reported	Hospital course

Table 2

Qualitative assessment of length of stay and operating room time.

Study (year)	Sample size per arm	EPI	PCA	Difference	Study arm favored	Statistical significance
Length of Stay		(days)	(days)	(days)		
St. Peter (2012)	55	4.5	4.3	0.2	PCA	NS p = 0.13
Butkovic (2007)	14	NR	NR	NR	NR	NR
Weber (2007)	20	8.4	9.5	1.1	EPI	NS
Reinoso - Barbero (2010)	22 EPI 9 PCA	NR	NR	NR	NR	NR
Soliman (2009)	9	5.1	4.4	0.7	PCA	NS
St. Peter (2008)	188 EPI 15 PCA	4.3	3.7	0.6	PCA	P = 0.037
		Qualitative Summary:			Favors PCA	
Operating Room Time		(minutes)	(minutes)	(minutes)		
St. Peter (2012)	55	118	95	23	PCA	NR p < 0.001
Butkovic (2007)	14	115	111	4	PCA	NS p > 0.05
Weber (2007)	20	96	97	1	EPI	NS
Reinoso - Barbero (2010)	22 EPI 9 PCA	NR	NR	NR	NR	NR
Soliman (2009)	9	261	328	67	EPI	NS
St. Peter (2008)	188 EPI 15 PCA	108	85	23	PCA	p = 0.004
		Qualitative Summary:			Favors PCA	

EPI = epidural arm; PCA = patient controlled analgesia arm; NR = not reported; NS = not significant.

Table 3

Qualitative description of epidural failures.

First author, year	Epidural failure rate	Qualitative description
St. Peter, 2012	22%	"6 patients were not able to have the EPI catheter placed successfully in the operating room, there were 6 additional patients who had the EPI catheter removed because of inadequate analgesia within the first 24 hours after the operation"
Butkovic, 2007	NR	No qualitative description provided by author
Weber, 2007	0%	"There was no technical difficulties during placement, and no epidural catheter had to be removed"
Reinoso–Barbero, 2010	0%	The author reports that no EPI catheter had to be removed before the pre-designated time
Soliman, 2009	0%	"No EPI catheter was discontinued prematurely"
St. Peter, 2008	35%	"there were 65 patients in whom the epidural catheter could not be placed, was technically tenuous, or was no longer functioning within 24 hours of surgery and removed" (59 placement failure in OR; 6 in postoperative care unit or floor)

EPI = epidural, NR = not reported; OR = operating room.