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SCIENTIFIC REVIEW

Milligan–Morgan (Open) Versus Ferguson Haemorrhoidectomy (Closed): A Systematic Review and Meta-Analysis of Published Randomized, Controlled Trials

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Abstract

Objective The purpose of this article is to systematically analyse the randomized, controlled trials (RCTs) comparing Ferguson or closed haemorrhoidectomy (CH) versus open haemorrhoidectomy (OH) or Milligan–Morgan haemorrhoidectomy in the management of haemorrhoidal disease (HD).

Methods RCTs on the effectiveness of CH and OH in the management of HD were analysed systematically using RevMan®, and combined outcome was expressed as odds ratio (OR) and standardized mean difference.

Results Eleven CRTs encompassing 1326 patients were analysed systematically. There was significant heterogeneity among included trials. Therefore, in the random effects model, CH was associated with a reduced post-operative pain (SMD, −0.36; 95 % CI, −0.64, −0.07; $z = 2.45$; $p = 0.01$), faster wound healing (OR, 0.08; 95 % CI, 0.02, 0.24; $z = 4.33$; $p < 0.0001$), lesser risk of post-operative bleeding (OR, 0.50; 95 % CI, 0.27, 0.91; $z = 2.27$; $p < 0.02$) and prolonged duration of operation (SMD, 6.10; 95 % CI, 3.21, 8.98; $z = 4.13$; $p < 0.0001$). But the variables such as pain on defecation (SMD, −0.33; 95 % CI, −0.68, 0.03; $z = 1.82$; $p = 0.07$), length of hospital stay, post-operative complications, HD recurrence and risk of surgical site infection were similar in both groups.

Conclusion CH has clinically measurable advantages over OH in terms of reduced post-operative pain, lower risk of post-operative bleeding and faster wound healing.

Introduction

The prevalence of haemorrhoidal disease (HD) ranges, according to different studies, from 4.4 to 86 % [1–4]. Surgical excision of advanced haemorrhoids in the form of haemorrhoidectomy has been reported with numerous complications. The major complications include sphincter dysfunction (up to 25 %), in 75 % cases pain, severe enough to eliminate patients from professional life for up to 3 weeks, bleeding in 5–15 % patients, and a 30 % risk of recurrent disease [4]. Despite these complications, haemorrhoidectomy is still considered an effective treatment of third-degree and fourth-degree haemorrhoids [5]. It can be performed by the

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open or closed technique [6, 7]. In Europe, the Milligan–Morgan procedure or open haemorrhoidectomy (OH) [6] is more frequently practised, whereas in the United States of America the closed haemorrhoidectomy (CH) procedure, as described by Ferguson and Heaton [7], is the most popular [8]. CH is purported to be a less painful procedure and associated with faster wound healing due to primary wound closure [6, 9–11]. However, the conflicting outcomes following both procedures have been debated in the published literature and several controversies with regards to post-operative pain still need clarification. The purpose of this article is to systematically analyse the randomized, controlled trials (RCTs) comparing CH versus OH in the management of HD.

Methods

Relevant prospective randomized, controlled trials (irrespective of type, language, gender, blinding, sample size or publication status) on CH versus OH for the management of HD until May 2014 were included in this review. The Cochrane Colorectal Cancer Group (CCCG) Controlled Trial Register, the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library, Medline, EMBASE and Science Citation Index Expanded were searched until May 2014 using the medical subject headings (MeSH) terms "third-degree haemorrhoids", "fourth-degree haemorrhoids", "prolapsing haemorrhoids" and "haemorrhoidal disease" in combination with "open haemorrhoidectomy", "Ferguson haemorrhoidectomy", "closed haemorrhoidectomy", "Milligan–Morgan haemorrhoidectomy" and "surgical haemorrhoidectomy" were searched. Boolean operators (AND, OR, NOT) were appropriately utilized to narrow and widen the search results. The published titles from the resultant search were scrutinized closely, and their suitability was determined for potential inclusion into this study. The references from selected published articles were also checked as a further search tool to find additional studies. For inclusion in the meta-analysis, a study had to meet the following criteria: (I) randomized, controlled trial; (II) comparison between CH and OH; (III) evaluation of post-operative pain; (IV) main outcome measures reported preferably as an intention-to-treat (ITT) analysis; and (V) trials in surgical patients who had undergone procedure for third-degree and fourth-degree haemorrhoids. Two reviewers using a predefined meta-analysis form extracted data from each study which resulted in satisfactory inter-observer agreement. The extracted data contained information regarding the name of the authors, title of the study, journal in which the study was published, country and year of the study, treatment regimen, length of the therapy, testing sample size (with sex differentiation if applicable), the number of patients receiving each regimen and within the group the number of patients who succeeded and the number of patients who failed the allocated treatment, the patient compliance rate in each group, the number of patients reporting complications and the number of patients with absence of complications in each arm.

The software package RevMan 5.2.12 [12, 13], provided by the Cochrane Collaboration, was used for the statistical analysis. The odds ratio (OR) with a 95 % confidence interval (CI) was calculated for binary data, and the standardized mean difference (SMD) with a 95 % CI was calculated for continuous variables. The random effects model [14, 15] was used to calculate the combined outcomes of both binary and continuous variables. Heterogeneity was explored using the chi^2 test, with significance set at $p < 0.05$, and was quantified [16] using I^2 test, with a maximum value of 30 % identifying low heterogeneity [16]. The Mantel–Haenszel method was used for the calculation of OR under the random effect models [17]. In a sensitivity analysis, 0.5 was added to each cell frequency for trials in which no event occurred in either the treatment or control group, according to the method recommended by Deeks et al. [18]. If the standard deviation was not available, then it was calculated according to the guidelines of the Cochrane Collaboration [12]. This process involved assumptions that both groups had the same variance, which may not have been true, and variance was either estimated from the range or from the p value. The estimate of the difference between both techniques was pooled, depending upon the effect weights in results determined by each trial estimate variance. A forest plot was used for the graphical display of the results. The square around the estimate stood for the accuracy of the estimation (sample size), and the horizontal line represented the 95 % CI. The methodological quality of the included trials was initially assessed using the published guidelines of Jadad et al. and Chalmers et al. [19, 20]. Based on the quality of the included randomized, controlled trials, the strength and summary of the evidence were further evaluated by GradePro® [21], a tool provided by the Cochrane Collaboration.

Results

The PRISMA flow chart explaining the outcome of electronic database search and methodology of included studies selection is given in Fig. 1. Eleven randomized, controlled trials [22–32] encompassing 1326 patients undergoing CH

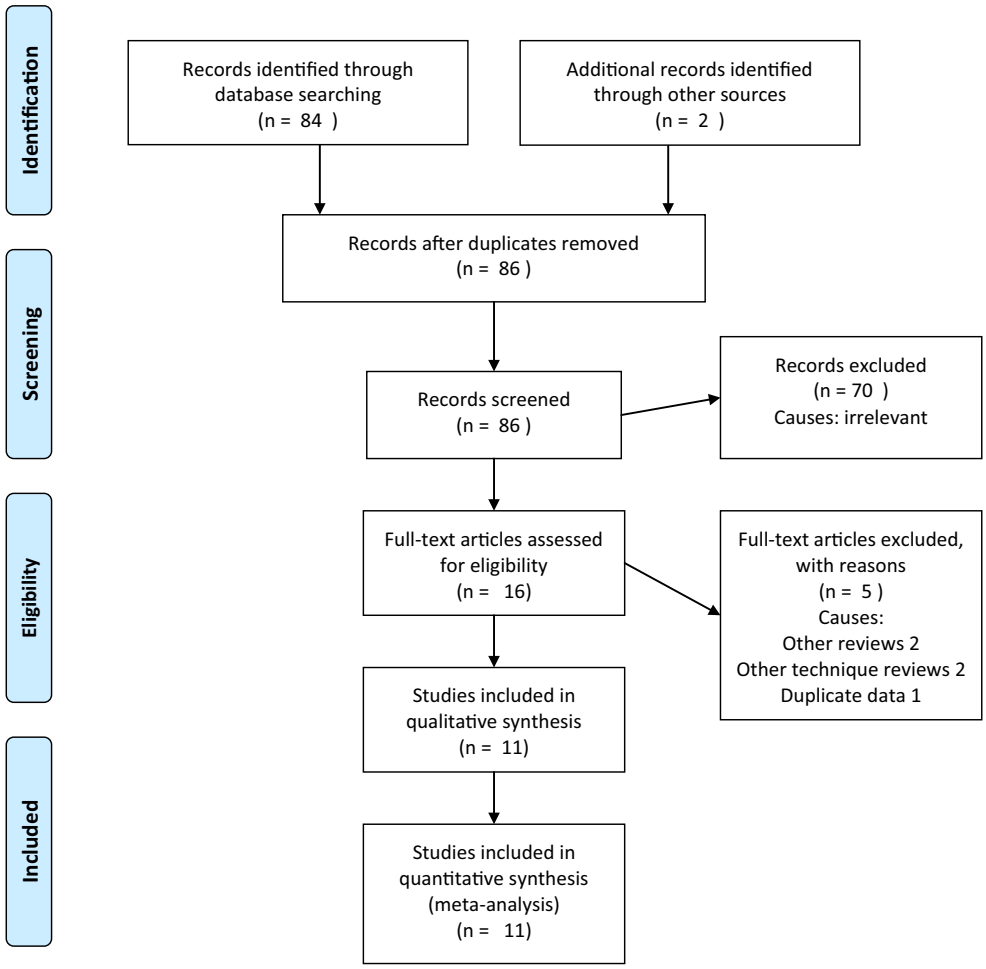

Fig. 1 PRISMA flow diagram

or OH for third-degree and fourth-degree haemorrhoids were retrieved from the electronic databases. Six hundred and sixty-three patients underwent CH and 663 patients underwent OH. The characteristics and treatment protocol adopted in included studies are given in Tables 1 and 2, respectively.

Methodological quality of included studies

The methodological quality of included trials (Table 3) was assessed by the published guideline of Jadad et al. and Chalmers et al. [19, 20]. Five trials [25, 26, 29–31] were of poor quality due to lack of adequate randomization technique, absence of blinding, lack of power calculations and in-adequate methods of concealment. Remaining six trials [22–24, 27, 28, 32] were considered of good quality due to adequate methodology following analysis of reported quality variables. Based on the quality of included randomized controlled trials, the strength and summary of evidence was further evaluated by GradePro® [21], a statistical tool provided by the Cochrane Collaboration [Fig. 2].

Post-operative pain score

Six included trials contributed to the combined calculation of this variable as shown in Fig. 3. There was significant heterogeneity [$Tau^2 = 0.14$, $chi^2 = 18.97$, $df = 5$, ($p = 0.002$); $I^2 = 74\ \%$] among trials. In the random effects model (SMD, −0.36; 95 % CI, −0.64, −0.07; $z = 2.45$; $p = 0.01$), the CH was associated with lower pain score post-operatively.

Duration of operation

Seven included trials contributed to the combined calculation of this variable as shown in Fig. 4. There was significant heterogeneity [$Tau^2 = 14.99$, $chi^2 = 873.05$,

Table 1 Characteristics of included studies

Trial	Country	Year	Age in years	Follow up in months	Disease stage
Arbman et al.	Sweden	2000	48(21–80)	12	II–IV degree haemorrhoids
CH					
OH					
Arroyo et al.	Spain	2004	43.5	12	I–IV degree haemorrhoids
CH					
OH					
Carapeti et al.	UK	1999	46(36–75)		Degree of haemorrhoids was not reported
CH			44(27–68)		
OH					
Gaj et al.	Italy	2007		6	III–IV degree haemorrhoids
CH					
OH					
Gencosmaoglu et al.	Turkey	2002	39.5(26–63)	19.5(4–40)	III–IV degree haemorrhoids
CH			40.5(27–68)		
OH					
Ho et al.	Singapore	1997	45 ± 1.7	8.7 ± 0.2	III–IV degree haemorrhoids
CH					
OH					
Johannsson et al.	Sweden	2006	53(27–82)	12	Degree of haemorrhoids was not reported
CH			52(22–82)		
OH					
Mik et al.	Poland	2008		18	III–IV degree haemorrhoids
CH					
OH					
Rehman et al.	Pakistan	2011	48.5(17–87)	6	III–IV degree haemorrhoids
CH					
OH					
Uba et al.	Nigeria	2004		3	II–III degree haemorrhoids
CH					
OH					
You et al.	South Korea	2005	41(25–74)	12	II–IV degree haemorrhoids
CH					
OH					

df = 6, ($p = 0.00001$); $I^2 = 99$ %] among trials. In the random effects model (SMD, 6.10; 95 % CI, 3.21, 8.98; z = 4.13; $p < 0.0001$), the CH was associated with longer duration of operation.

Pain on defecation

Four included trials contributed to the combined calculation of this variable as shown in Fig. 5. There was significant heterogeneity [$\text{Tau}^2 = 0.09$, $\text{chi}^2 = 10.90$, df = 3, ($p = 0.01$); $I^2 = 72$ %] among trials. In the random effects model (SMD, −0.33; 95 % CI, −0.68, 0.03; $z = 1.82$; $p < 0.07$), the pain scores were statistically similar following both CH and OH.

Length of hospital stay

Eleven included trials contributed to the combined calculation of this variable as shown in Fig. 6. There was significant heterogeneity [$\text{Tau}^2 = 0.35$, $\text{chi}^2 = 105.88$, df = 10, ($p = 0.00001$); $I^2 = 91$ %] among trials. In the random effects model (SMD, −0.36; 95 % CI, −0.73, 0.01; $z = 1.89$; $p < 0.06$), the length of hospital stay was statistically similar following both CH and OH.

Table 2 Treatment protocol adopted in included studies

Trial	Closed haemorrhoidectomy group	Open haemorrhoidectomy group
Arbman et al.	Jack knife position	Lithotomy position
	Elliptical incision and scissors dissection	Pear shaped incision and scissors dissection up to dentate line where pedicle was ligated
	Partial open sphincterotomy	Wound was left open
	Wound closed with 5/0 polyglycolic acid continuous suture	Regional anaesthesia and standard analgesia
	Regional anaesthesia and standard analgesia	
Arroyo et al.	Local anaesthetic in haemorrhoidal cushion	Same as except wound was not closed
	Diathermy dissection to base then pedicle ligation	Standard post-operative care in both arms
	Wound closure with 3/0 polyglycolic acid continuous suture	General, regional or spinal anaesthetic was used depending upon patient choice
Carapeti et al.	Procedure protocol was not reported	Procedure protocol was not reported
Gaj et al.	Not available	Not available
Gencosmaoglu et al.	Local anaesthetic with adrenalin in haemorrhoidal cushion	Local anaesthetic in haemorrhoidal cushion
	Diathermy dissection to base then pedicle ligation	Diathermy dissection to base then ligation of the pedicle
	Wound closure with 3/0 polyglactin continuous suture	Wound was not closed
Ho et al.	Procedure was performed under general or spinal anaesthetic	Diathermy dissection to base but base was not ligated
	Diathermy dissection to base then pedicle ligation	Wound was not closed
	Wound closure with 3/0 polyglactin continuous suture	
Johannsson et al.	Diathermy or scissors for dissection	Procedure protocol was not reported
	Pedicle ligation by ligature	Wound was not closed
	4/0 polyglycolic acid for wound closure	Both sphincters were identified
	Both sphincters were identified	6 patients had sphincterotomy
	5 patients had sphincterotomy	One patient had anal dilatation
	Local anaesthetic was used in selected patients	Local anaesthetic was used in selected patients
Mik et al.	Not available	Not available
Rehman et al.	Procedure protocol was not reported	Procedure protocol was not reported
Uba et al.	Wound closed with 5/0 chromic catgut	
You et al.	Procedure was performed under general or spinal anaesthetic	Diathermy dissection to base but base was not ligated
	Diathermy dissection to base then pedicle ligation	Wound was not closed
	Wound closure with 3/0 polyglactin continuous suture	

Post-operative complications

Eleven included trials contributed to the combined calculation of this variable as shown in Fig. 7. There was significant heterogeneity [$Tau^2 = 0.57$, $chi^2 = 24.97$, $df = 9$, ($p = 0.003$); $I^2 = 64$ %] among trials. In the random effects model (OR, 0.81; 95 % CI, 0.44, 1.48; $z = 0.69$; $p = 0.49$), the risk of post-operative complications was similar in both groups.

Post-operative bleeding

Eleven included trials contributed to the combined calculation of this variable as shown in Fig. 8. There was no heterogeneity [$Tau^2 = 0.12$, $chi^2 = 7.17$, $df = 6$, ($p = 0.31$); $I^2 = 16$ %] among trials. In the random effects model (OR, 0.50; 95 % CI, 0.27, 0.91; $z = 2.27$; $p = 0.02$), the risk of post-operative bleeding was higher following OH.

Table 3 Reported quality variables in included studies

Trial	Randomization	Power calculations	Blinding	Concealment	Intention-to-treat
Arbman et al.	Random numbers allocation	Not reported	Not reported	Not reported	Not reported
Arroyo et al.	Random allocation	Not reported	Not reported	Not reported	Not reported
Carapeti et al.	Consecutive patients	Yes	Not reported	Not reported	Not reported
Gaj et al.	Not reported	Not reported	Not reported	Not reported	Not reported
Gencosmaoglu et al.	Random allocation	Not reported	Not reported	Not reported	Not reported
Ho et al.	Not reported	Not reported	Yes	Not reported	Not reported
Johannsson et al.	Random numbers in envelops	Yes	Not reported	Yes	Yes
Mik et al.	Not available	Not available	Not available	Not available	Not available
Rehman et al.	Random allocation	Not reported	Not reported	Not reported	Not reported
Uba et al.	Not reported	Not reported	Not reported	Not reported	Not reported
You et al.	Random number generation	Yes	No	Yes	Not reported

Surgical site infection

Eleven included trials contributed to the combined calculation of this variable as shown in Fig. 9. There was no heterogeneity [$Tau^2 = 0.0$, $chi^2 = 3.76$, $df = 4$, ($p = 0.44$); $I^2 = 0$ %] among trials. In the random effects model (OR, 2.21; 95 % CI, 0.66, 7.39; $z = 1.28$; $p = 0.20$), the risk of post-operative surgical site infection was similar in both groups.

Delayed wound healing

Eleven included trials contributed to the combined calculation of this variable as shown in Fig. 10. There was significant heterogeneity [$Tau^2 = 1.90$, $chi^2 = 34.02$, $df = 7$, ($p = 0.0001$); $I^2 = 79$ %] among trials. In the random effects model (OR, 0.08; 95 % CI, 0.02, 0.24; $z = 4.33$; $p < 0.0001$), the risk of delayed wound healing was higher following OH.

Recurrence

Eleven included trials contributed to the combined calculation of this variable as shown in Fig. 11. There was no heterogeneity [$Tau^2 = 0.00$, $chi^2 = 1.22$, $df = 3$, ($p = 0.75$); $I^2 = 0$ %] among trials. In the random effects model (OR, 0.91; 95 % CI, 0.56, 1.48; $z = 0.38$; $p = 0.70$), the risk of HD recurrence was similar in both groups.

Discussion

Based upon the findings of this review CH was associated with a reduced post-operative pain, faster wound healing, lesser risk of post-operative bleeding but prolonged duration of operation. The variables such as pain on defecation, length of hospital stay, post-operative complications, HD recurrence and the risk of surgical site infection were similar in both groups. Therefore, it is fair to conclude that CH has shown clinically measurable advantages over OH for reduced post-operative pain, lower risk of post-operative bleeding and faster wound healing. Findings of this review are contradictory to previously published meta-analysis of six randomized, controlled trials [33]. Study published by Ho et al. in 2007 advocated the faster wound healing and failed to demonstrate other potential advantages of CH. However, current review of eleven randomized, controlled trials on 1326 patients validated the previously reported variable of faster wound healing in addition to the lower post-operative pain, reduced risk of post-operative bleeding with slightly longer duration of operation.

The included randomized, controlled trials evaluated post-operative pain as primary or secondary outcomes according to the pre-trial analysis strategy. The use of post-operative pain as primary or secondary endpoints following CH or OH was well targeted because the post-operative pain is a major burden of morbidity in patients undergoing HD surgery. This outcome was thoroughly investigated and adequately reported in included randomized, controlled trials. However, present review still has some limitations. Studies included in this review that recruited a small number of patients may not have had sufficient power to reveal small differences in outcomes. Due to fewer numbers of patients and fewer trials on this subject, it is still unwise to generalize the results of this study to all groups of patients undergoing HD surgery. Six included studies were of poor methodological quality. The major methodological flaws in included trials were the lack of a uniformed and standardized pain measuring tool. The surgeons performing procedure were of variable experience

Closed haemorrhoidectomy for haemorrhoidal disease

Patient or population: patients with haemorrhoidal disease
Settings:
Intervention: Closed haemorrhoidectomy

Outcomes	Illustrative comparative risks* (95% CI) Assumed risk Control	Corresponding risk Closed haemorrhoidectomy	Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
Duration of operation Standardised mean difference Follow-up: 2-24 months		The mean duration of operation in the intervention groups was **6.1 standard deviations higher** (3.21 to 8.98 higher)		924 (7 studies)	⊕⊕⊕⊖ **moderate**	SMD 6.1 (3.21 to 8.98)
Postoperative pain Standardised mean difference Follow-up: 2-24 months		The mean postoperative pain in the intervention groups was **0.36 standard deviations lower** (0.64 to 0.07 lower)		809 (6 studies)	⊕⊕⊕⊖ **moderate**	SMD -0.36 (-0.64 to -0.07)
Pain on defecation Standardised mean difference Follow-up: 2-24 months		The mean pain on defecation in the intervention groups was **0.33 standard deviations lower** (0.68 lower to 0.03 higher)		507 (4 studies)	⊕⊕⊕⊖ **moderate**	SMD -0.33 (-0.68 to 0.03)
Length of hospital stay Standardised mean difference Follow-up: 2-24 months		The mean length of hospital stay in the intervention groups was **0.36 standard deviations lower** (0.73 lower to 0.01 higher)		1326 (11 studies)	⊕⊕⊕⊖ **moderate**	SMD -0.36 (-0.73 to 0.01)
Operative complications Odds ratio Follow-up: 2-24 months	Study population 195 per 1000 Moderate 147 per 1000	 **164 per 1000** (96 to 263) **122 per 1000** (70 to 203)	**OR 0.81** (0.44 to 1.48)	1326 (11 studies)	⊕⊕⊕⊖ **moderate**	
Bleeding Odds ratio Follow-up: 2-24 months	Study population 113 per 1000 Moderate 25 per 1000	 **60 per 1000** (33 to 104) **13 per 1000** (7 to 23)	**OR 0.5** (0.27 to 0.91)	1326 (11 studies)	⊕⊕⊕⊖ **moderate**	
Wound infection Odds ratio Follow-up: 2-24 months	Study population 5 per 1000 Moderate 0 per 1000	 **10 per 1000** (3 to 32) **0 per 1000** (0 to 0)	**OR 2.21** (0.66 to 7.39)	1326 (11 studies)	⊕⊕⊕⊖ **moderate**	
Delayed wound healing Odds ratio Follow-up: 2-24 months	Study population 354 per 1000 Moderate 231 per 1000	 **42 per 1000** (11 to 116) **23 per 1000** (6 to 67)	**OR 0.08** (0.02 to 0.24)	1326 (11 studies)	⊕⊕⊕⊖ **moderate**	
Recurrence Odds ratio Follow-up: 2-24 months	Study population 65 per 1000 Moderate 0 per 1000	 **59 per 1000** (37 to 93) **0 per 1000** (0 to 0)	**OR 0.91** (0.56 to 1.48)	1326 (11 studies)	⊕⊕⊕⊖ **moderate**	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **OR:** Odds ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Fig. 2 Summary and strength of the evidence from trials analysed on GradePro®

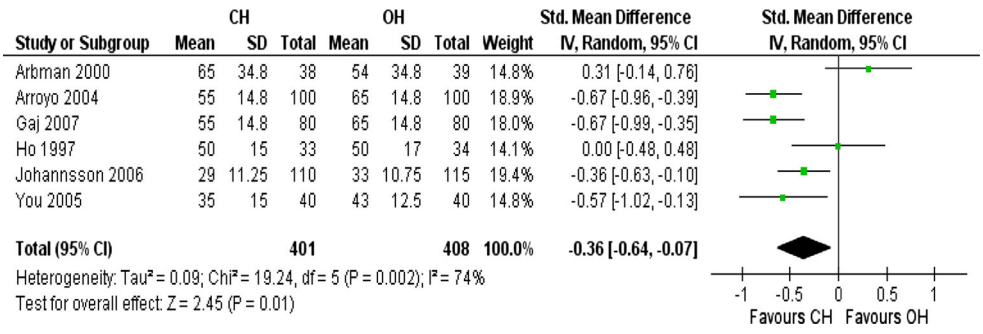

Fig. 3 Forest plot for post-operative pain score following CH versus OH. Standardized mean differences are shown with 95 % confidence intervals. *CH* closed haemorrhoidectomy, *OH* open haemorrhoidectomy

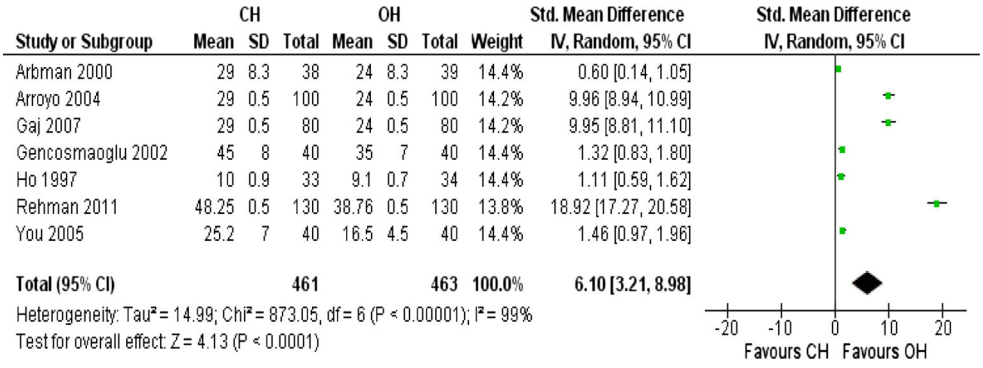

Fig. 4 Forest plot for duration of operation following CH versus OH. Standardized mean differences are shown with 95 % confidence intervals. *CH* closed haemorrhoidectomy, *OH* open haemorrhoidectomy

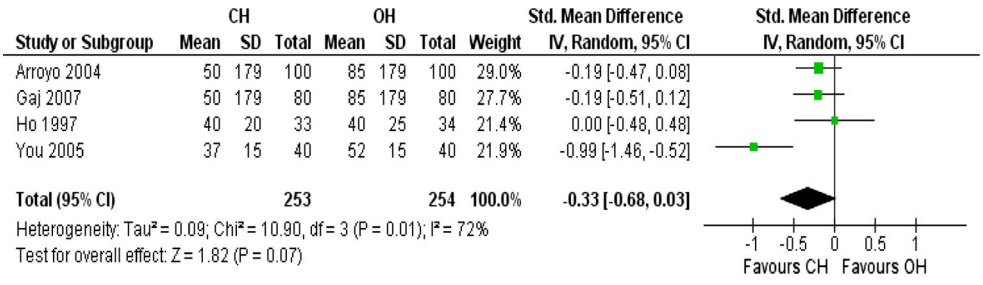

Fig. 5 Forest plot for pain on defecation following CH versus OH. Standardized mean differences are shown with 95 % confidence intervals. *CH* closed haemorrhoidectomy, *OH* open haemorrhoidectomy

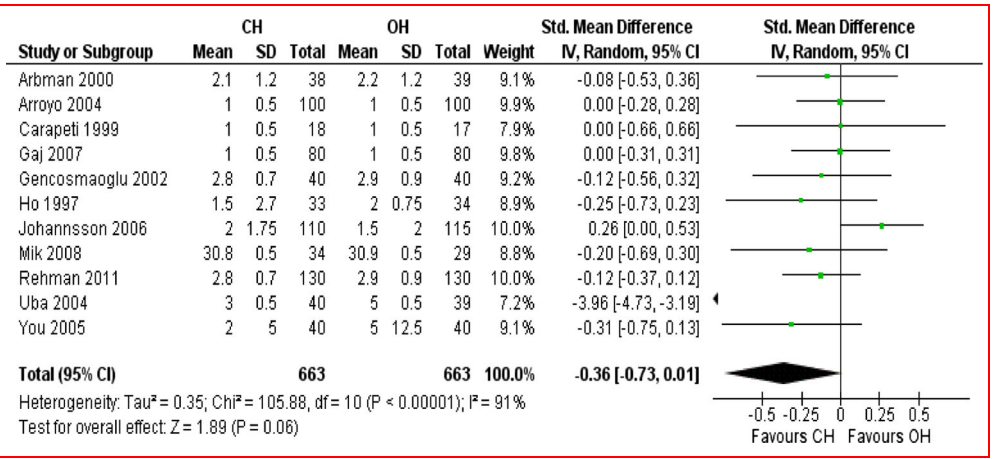

Fig. 6 Forest plot for length of hospital stay following CH versus OH. Standardized mean differences are shown with 95 % confidence intervals. *CH* closed haemorrhoidectomy, *OH* open haemorrhoidectomy

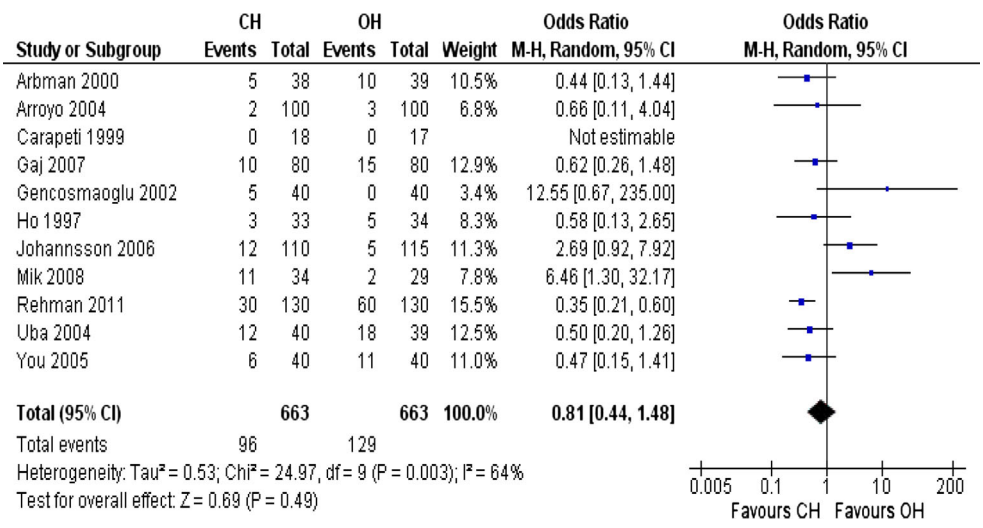

Fig. 7 Forest plot for post-operative complications following CH versus OH. Odds ratios are shown with 95 % confidence intervals. *CH* closed haemorrhoidectomy, *OH* open haemorrhoidectomy

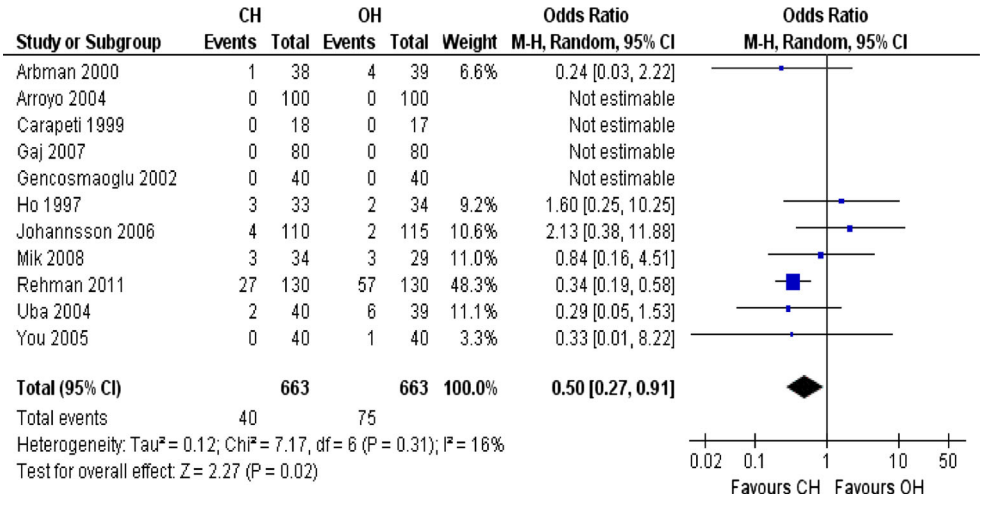

Fig. 8 Forest plot for post-operative bleeding following CH versus OH. Odds ratios are shown with 95 % confidence intervals. *CH* closed haemorrhoidectomy, *OH* open haemorrhoidectomy

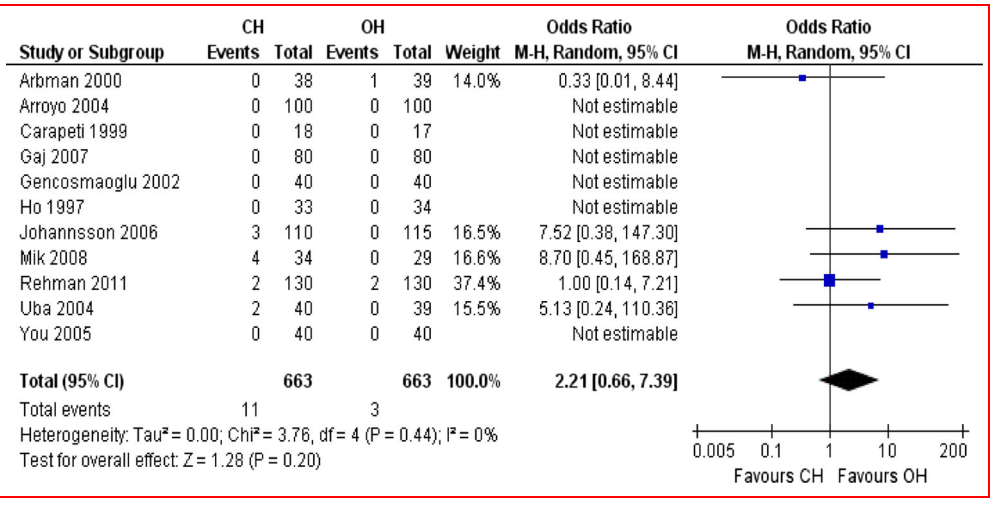

Fig. 9 Forest plot for surgical site infection following CH versus OH. Odds ratios are shown with 95 % confidence intervals. *CH* closed haemorrhoidectomy, *OH* open haemorrhoidectomy

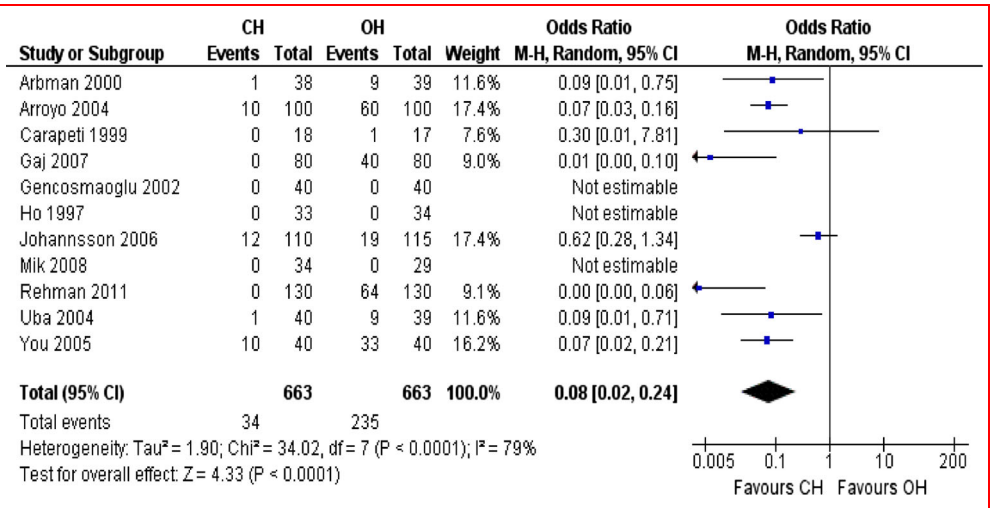

Fig. 10 Forest plot for delayed wound healing following CH versus OH. Odds ratios are shown with 95 % confidence intervals. *CH* closed haemorrhoidectomy, *OH* open haemorrhoidectomy

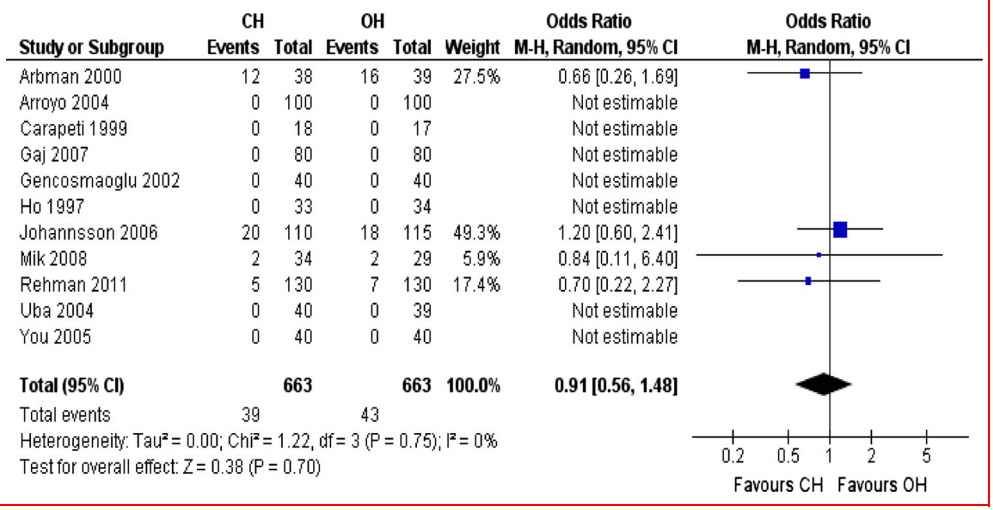

Fig. 11 Forest plot for recurrence following CH versus OH. Odds ratios are shown with 95 % confidence intervals. *CH* closed haemorrhoidectomy, *OH* open haemorrhoidectomy

and operator dependent pain score differences were not reported adequately. Therefore, a major multicentre, high powered, randomized, controlled trial is mandatory to validate the findings of this review and until then current study may assist colorectal surgeons in decision making about which technique should be adopted to perform haemorrhoidectomy for third-degree and fourth-degree haemorrhoids.

Authors Contribution Study conception: Mr MS Sajid, MBBS, MBA, MSc, FRCS, Specialist Registrar Colorectal Surgery; Mr MK Baig, MBBS, MD, FRCS, Consultant Colorectal Surgeon. Design: Mr MS Sajid, Mr MI Bhatti, MBBS, FRCS, Specialist Registrar Colorectal Surgery. Literature search: Mr MS Sajid, Mr MI Bhatti. PRISMA flow chart for study selection: Mr MS Sajid, Mr MI Bhatti, Mr MK Baig. Data acquisition: Mr MS Sajid, Mr I Bhatti. Data confirmation: Mr MK Baig. Data analysis: Mr MS Sajid, Mr MK Baig, Mr I Bhatti. Data interpretation: Mr MS Sajid, Mr MK Baig, Mr WFA Miles, Mr MI Bhatti. Proofreading of the article: Mr MK Baig. Final approval of the version to be published: Mr MS Sajid, Mr MI Bhatti, Mr MK Baig.

Compliance with ethical standards

Conflict of Interest None to declare.

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