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SCIENTIFIC REVIEW

Prophylactic Mesh After Midline Laparotomy: Evidence is out There, but why do Surgeons Hesitate?

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Abstract

Background Incisional hernias have an impact on patients' quality of life and on health care finances. Because of high recurrence rates despite mesh repair, the prevention of incisional hernias with prophylactic mesh reinforcement is currently a topic of interest. But only 15% of surgeons are implementing it, mainly because of fear for mesh complications and disbelief in the benefits. The goal of this systematic review is to evaluate the effectiveness and safety of prophylactic mesh in adult patients after midline laparotomy.

Methods An extensive literature search was performed in PubMed, Embase and CENTRAL until 9/5/2020 for RCTs and cohort studies regarding mesh reinforcement versus primary suture closure of a midline laparotomy. The quality of the articles was analyzed using the Scottish Intercollegiate Guidelines Network checklists. Revman 5 was used to perform a meta-analysis.

Results Twenty-three articles were found with a total of 1633 patients in the mesh reinforcement group and 1533 in the primary suture group. An odds ratio for incisional hernia incidence of 0.37 (95% CI = [0.30, 0.46], $p < 0.01$) with RCTs and of 0.15 (95% CI = [0.09,0.25], $p < 0.01$) in cohort studies was calculated. Seroma rate shows a significant odds ratio of 2.18 (95% CI = [1.45, 3.29], $p < 0.01$) in favor of primary suture. No increase was found regarding other complications.

Conclusion The evidence for the use of prophylactic mesh reinforcement is overwhelming with a significant reduction in incisional hernia rate, but implementation in daily clinical practice remains limited. Instead of putting patients at risk for incisional hernia formation and subsequent complications, surgeons should question their arguments why not to use mesh reinforcement, specifically in high-risk patients.

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Introduction

Abdominal wall hernias have a negative impact on patient's quality of life. They might cause pain, obstruction, incarceration (6–15%), strangulation (2%) as well as aesthetic complaints [1–4]. Furthermore, they have financial consequences for both patient and society. The average additional medical expenditure for patients that do develop incisional hernias (IH) versus patients that don't, is between $21,211 and $28,870 [5].

Incisional hernias occur in 2–50% of the patients that underwent open midline laparotomy and even in 70% in high-risk patients. Obesity and connective tissue disorders are the most important risk factors, but more are identified, like COPD, chronic steroid use and infection [6–9]. Recurrence rates of 25–63% after primary suture (PS) repair and 11–32% for mesh repair still apply [10, 11]. Because of these high recurrence rates, the prevention of incisional hernias with prophylactic mesh reinforcement (PMR) might have a great impact. Although about 89% of surgeons are familiar with the current literature, the most frequent reason why surgeons are reluctant to use prophylactic mesh, is fear for mesh infection and complications. [12]. Infection may lead to chronic wound problems, subsequent mesh removal and lowers the success rate of a later hernia repair [11]. Also a slight increase in operation time is considered with a mean of 15 min [3, 13]. Other reasons why they are rather skeptical regarding potential benefits of PMR are unfamiliarity with the surgical technique and financial loss [12].

After discussion with the patient, the best location of the mesh might be questioned too. Both sublay and onlay mesh position are widely used in abdominal wall reconstruction. The onlay position is easier to perform, but needs creation of larger skin flaps. The sublay position is more technically demanding, but is physiological, shows low recurrence and decreased SSI rates in hernia repair [14].

Because of this ongoing debate about the pros and cons of mesh reinforcement, as well as the difficult implementation in daily practice by general surgeons, this review tries to summarize the current evidence on prophylactic mesh placement after midline laparotomy.

Material and methods

An extensive literature search was performed in PubMed, Embase and Cochrane Central Register of Controlled Trials (CENTRAL) until 9/5/2020 for RCT's and cohort studies (Fig. 1 [15]). Following MeSH-terms were used: Surgical Mesh, Hernia, Abdominal OR Hernia, Ventral OR Hernia, Umbilical (prevention and control), Midline laparotomy, Obesity and Aortic Aneurysm, Abdominal. Other relevant articles were also selected from review citations. This was performed by 2 independent reviewers (D.M., B.F.). In a first-level screening, only studies about prophylactic use of meshes in laparotomy in humans were screened for. Studies concerning parastomal, inguinal and hernia repair were excluded. In a second-level screening, the quality of the articles was analyzed using the checklists of the Scottish Intercollegiate Guidelines Network (SIGN) [16–18]. Low quality studies were excluded. Data were extracted in an extraction sheet, similar to Tables 1 and 2. The primary outcome is the effect on the incidence of incisional hernias. The secondary outcomes are complications as seroma, infection and chronic pain.

The PMA group was selected as intervention group and the PS group as the control group. Patient demographic similarity was reported in the studies. A fixed-effect model was used to pool data. The outcomes were dichotomous, and odds ratios were calculated with the Mantel–Haenszel method with a 95% confidence interval. Subgroup analysis was performed with studies that reported infection rate, seroma rate and chronic pain assessment. Heterogeneity was assessed with Chi^2 and I^2. $p < 0.05$, and $I^2 > 50\%$ heterogeneity was seen as significant heterogeneity. This was performed using Review Manager 5 (*The Cochrane Collaboration, Copenhagen*). The research is being reported in line with the guidelines of Moher et al. [15] and Probst et al. [19].

Results

In total, 23 articles were found regarding PMR: 17 studies are RCTs, and 6 are cohort studies. Two articles report on long-term results of previously published data by the same authors. Fifteen studies have high quality, and 8 have acceptable quality according to SIGN-checklist [16–18]. The studies include a total of 1633 patients in the PMR group and 1533 in the PS group. The characteristics of the included studies can be found in Table 1, while the results are summarized in Table 2.

The design of most studies is comparable for both PMR and PS closing techniques after midline laparotomy. All but one [20] used slowly- or non-absorbable running sutures. Ten authors mentioned recommending a suture length-to-wound length ratio of 4:1 but this was never measured [21]. Ten authors reported closing with a 1 cm distance between stiches and 1 cm distance to the fascial border. Others mentioned standard fascia closure without specifying the technique. Note that currently smaller bites of 0.5 cm are recommended, the so-called small bites, small steps technique [21, 22]. Nine out of the 23 authors used sublay, 11 used onlay, 1 both sublay and onlay, 1

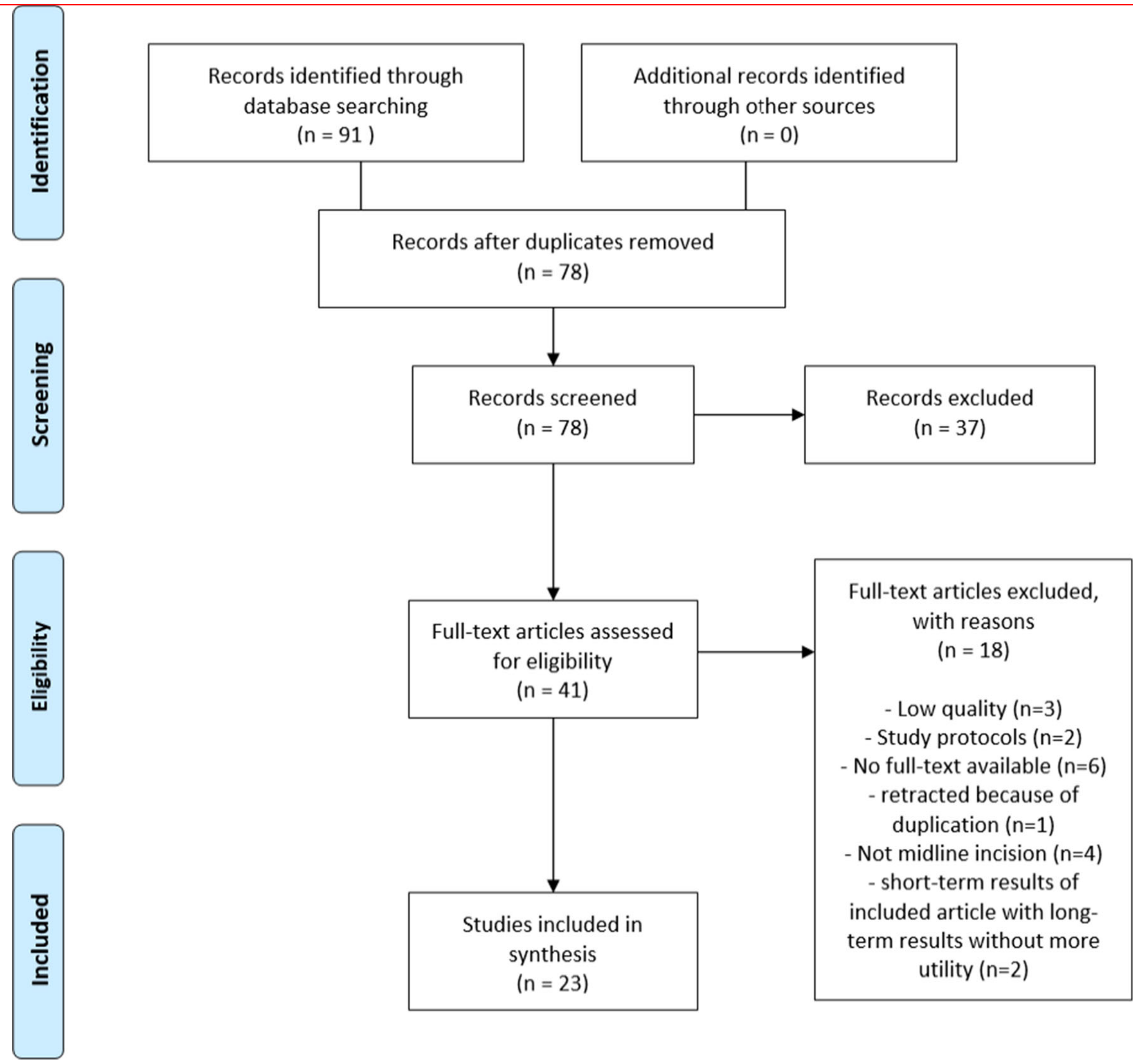

Fig. 1 PRISMA for studies concerning IH prevention after laparotomy [15]

inlay and 1 intraperitoneal mesh placement. Four studies used biological mesh, while all others used a synthetic polypropylene mesh. The most important differences between studies concern both methodology and duration of follow-up. Subgroup analysis of different techniques could not be properly performed because of lack of adequate data.

The meta-analysis including all RCTs shows a difference in incisional hernia formation of 13.6% for the PMR group versus 28.1% for the PS group with a significant odds ratio (OR) of 0.37 (95% CI = [0.30, 0.46] (Fig. 2). The risk ratio of having an incisional hernia when implementing PMR in comparison of PS is 0.46, (95% CI = [0.38, 0.55]). (Table 3) There was a significant statistical heterogeneity of 64% between the studies. The cohort studies also show a significant odds ratio of 0.15 (95% CI = [0.09,0.25]) (Fig. 3) without heterogeneity.

Fourteen RCTs and five cohort studies published data on infection, both superficial, deep and mesh infection. There was no difference in overall infection in RCTs (OR = 1.00, 95% CI = [0.74, 1.35]) (Fig. 4) and cohort studies (OR = 1.19, 95% CI = [0.76, 1.86]). (Fig. 5) Twelve RCTs reported data on seroma and showed significantly more seroma formation in the PMR group than in the PS group (OR = 2.18, 95% CI = [1.45, 3.29]). (Fig. 6) The cohort studies could not be analyzed for this complication due to insufficient data. Only 5 studies reported the treatment of seromas [7, 9, 23–25]. Out of 75 seromas reported, only 1 was reoperated because of suspicion of infection. All others were treated non-surgically, with or without percutaneous drainage. Only 6 RCTs investigated chronic pain, with a significant increase in the PMR group with an OR of 1.68 (95% CI = [1.02, 2.76]), without heterogeneity (Fig. 7).

Table 1 Study characteristics of the included studies

Study	Blindness*	N (PMR/PS)	Follow-up (months)	Mesh technique/type	Suture technique	Follow-up method	Indication
Abo-Ryia et al, [49]	U	64 (32/32)	48	Sublay, lightweight, polypropylene large-pore	Non-absorbable running suture, 1 cm bites	Clinical examination and/or ultrasound	Obesity (bariatric surgery)
Bali et al, [9]	U	40 (20/20)	36	Onlay, bioprosthesis	Slowly-absorbable running suture, 4:1	Clinical examination and CT	AAA
Bevis et al.[23]	S	85 (40/45)	25	Sublay, lightweight, polypropylene large-pore	Non-absorbable running suture, 4:1	Clinical examination and ultrasound	AAA
Brosi et al. [28]	O	267 (131/136)	24	Onlay, lightweight, large-pore, partially absorbable	Slowly-absorbable running suture, 4:1, 1 cm bites	Clinical examination and ultrasound	General
Caro-Tarrago et al. [50]	S	160 (80/80)	12	Onlay, lightweight, polypropylene, large-pore	Slowly-absorbable running suture, 4:1, 1 cm bites	CT	General
Caro-Tarrago et al. [24]	S	160 (80/80)	60	Onlay, lightweight, polypropylene, large-pore	Slowly-absorbable running suture, 4:1, 1 cm bites	CT	General
El-Khadrawy et al. [51]	U	40 (20/20)	37	Sublay, lightweight, polypropylene large-pore	Non-absorbable running suture, 1 cm bites	Clinical examination and ultrasound	$>$ 1 risk factors
Garcia-Urena et al. [34]	S	107 (53/54)	24	Onlay, lightweight, polypropylene, large-pore	Slowly-absorbable running suture, 4:1, 1 cm bites	CT	General
Glauser et al. [41]	O	267 (131/136)	63	Onlay, lightweight, large-pore, partially absorbable	Slowly-absorbable running suture, 4:1, 1 cm bites	Clinical examination and ultrasound	General
Gutierrez De La Pena et al. [35]	U	88 (44/44)	36	Onlay, lightweight, polypropylene large-pore	Non-absorbable running suture, 1 cm bites	Clinical examination and/or CT	$>$ 1 of: malignancy, $>$ 70y, resp failure, malnutrition, BMI $>$ 30, smoker
Jairam et al. [7]	D	480 (188 (oPMR)/ 185(sPMR) /107 (PS)	24	Onlay vs sublay, lightweight, polypropylene large-pore	Slowly-absorbable running suture, 4:1	Clinical examination and CT	AAA/ BMI $\geq$ 27 kg/m^2
Kohler et al. [30]	O	169 (83/86)	36	Onlay, lightweight, large-pore, partially absorbable	Slowly-absorbable running suture, 1 cm bites	Clinical examination and/or imaging	$\geq$ 2 of: obesity, malignity, male or re-operation

Table 1 continued

Study	Blindness*	N (PMR/PS)	Follow-up (months)	Mesh technique/type	Suture technique	Follow-up method	Indication
Muysoms et al. [25]	O	114 (56/58)	24	Sublay, lightweight, polypropylene large-pore	Slowly-absorbable running suture, 4:1	Ultrasonography and/or CT	AAA
Pans et al. [20]	U	288 (144/144)	30	Sublay, polyglactin	Absorbable, interrupted suture	Clinical examination	Obesity (bariatric surgery)
Pizza et al. [52]	D	92 (45/47)	24	Sublay, biosynthetic strip	Slowly-absorbable running suture, 4:1	Clinical examination and ultrasonography	General
Sarr et al. [13]	U	380 (185/195)	24	Sublay, bioprosthesis,	Slowly-/non-absorbable running suture	Clinical examination and/or imaging	BMI $\geq$ 40 kg/m^2 or@BMI $\geq$ 35 kg/m^2 + comorbidity
Strzelczyk et al. [53]	S	74 (36/38)	28	Sublay, lightweight, polypropylene large-pore	Non-absorbable running suture	Clinical examination and ultrasound	Obesity (bariatric surgery)
Argudo et al. [54]	N/A	150 (51/99)	12	Onlay, low weight, partly absorbable polypropylene, large-pore	Slowly-absorbable running (+ retention suture)	Clinical examination and/or imaging	Emergency operation
Argudo et al. [31]	N/A	226 (160/66)†	31.5	Onlay, lightweight, large-pore, partially absorbable	Slowly-absorbable running suture	Clinical examination and/or CT-scan	HERNIAscore > 7††
Curro et al. [27]	N/A	95 (45/50)	24	Sublay, lightweight, polypropylene large-pore	Absorbable running suture	Clinical examination and ultrasound	Obesity (bariatric surgery)
Kurmann et al. [55]	N/A	133 (63/70)	16	Intraperitoneal polypropylene, large-pore	Slowly-absorbable running suture, 4:1, 1 cm bites	Clinical examination and/or imaging	Peritonitis + $\geq$ 2 of: male, BMI $\geq$ 25 kg/m^2, malignity, previous incision
Llaguna et al. [56]	N/A	106 (44/62)	24	Inlay, biological mesh	Slowly-absorbable running suture, 1 cm bites	Clinical examination	Obesity (bariatric surgery)
Von Ahrens et al. [57]	N/A	111 (26/85)	22	Onlay, absorbable mesh	Not specified	Not specified	BMI $\geq$ 27

* S = Single, D = Double, O = Open label, U = Unknown, N/A = Not applicable

† No algorithm vs following algorithm for mesh placement

†† 4 × laparotomy + 3 × Hand-assisted laparoscopy + 1 × COPD + 1 × BMI > 25

Discussion

Post-operative incisional hernias are an important health care problem and can result in high morbidity and even mortality. Risk factors like obesity and AAA can raise the risk to 70% after laparotomy. However, IHs appear to generate little interest: at the end of an operation 'closing time' is sometimes viewed as 'coffee time' or is done by less experienced and trained surgical residents [26]. Various solutions have been advocated, such as closure using a small bite technique and prophylactic mesh reinforcement (PMR) [27]. Awareness as well as debate regarding the use of prophylactic mesh have now gained more attention, but implementation is still very low [12]. Prevention of IH

Table 2 Study results of the included studies

Study	IH incidence (PMR/PS) (%)	Infection (PMR/PS) (%)	Chronic pain (PMR/PS) (%)	Seroma (PMR/PS) (%)	Other results (PMR/PS)
Abo-Ryia et al. [49]	3.1/ 28.1, p < 0.01*	Wound: 37/37, $p > 0.05$	N/A	6/5, $p > 0.05$	
Bali et al. [9]	0/31.6, log rank $p = 0.008$*	Wound: 0/0, $p > 0.05$ MeSH: 0	N/A	5/10, $p = 1$	Operative time: 143–219 vs 104–158 min, $p < 0.001$* Mesh removal: 0%
Bevis et al. [23]	14/37, $p = 0.022$*	5/4.4, $p = 1$	/	5/0	
Brosi et al. [28]	1739, $P < 0.001$*	3.1/0.7, $p > 0.05$	0.25/0.27, $p > 0.05$	1.5/1.5, $p > 0.05$	Re-operation hernia: 11% vs 23%, $p < 0.02$ Minor adhesion
Caro-Tarrago et al. [50]	1.5/35.9, $p < 0.001$*	12.6/11.3, $p = 0.88$	N/A	28.8/ 11.3, $p < 0.01$*	Mesh removal: 0%
Caro-Tarrago et al. [24]	5.1/46.8, $P < 0.001$*	0/ 0	0/0	5y: 0/0	Obesity not-sign risk
El-Khadrawy et al. [51]	5/15, $p = 0.01$*	10/20, $p > 0.05$	15/ 0	20/15, $p > 0.05$	
Garcia-Urena et al. [34]	11.3/ 31.5, $p = 0.011$*	Wound: 18.9/33.3, $p = 0.12$ MeSH: 0	N/A	N/A	NNT = [3, 16] Incidence:—1% = + $32 million Mesh removal: 0%
Glauser et al. [41]	27.4/52.3, $p < 0.001$*	3.1/0.7, $p > 0.05$	N/A	1.5/1.5, $p > 0.05$	
Gutierrez De La Pena et al. [35]	0/11,4, $p = 0.02$*	2.2/2.2, $p > 0.05$	4.5/0, $p > 0.05$	2.2/6.8, $p > 0.05$	
Jairam et al. [7]	PS > PMR, $p = 0.003$* PS > oPMR, $p = 0.002$* PS > sPMR p = 0.05 sPMR > oPMR, $p = 0.31$	Wound: 13.1 (PS) vs 18.6 (oPMR) vs 10.3 (sPMR), $p > 0.05$ MeSH: 1.6	79.49/77.79, $p = 0.60$ (mean score, range 0–100)	oPMR (18.1) vs PS (4.7)/sPMR (7) ($p \leq 0.002$)*	Subcutaneous suture: oPMR (37.2%) vs PS (16.8%)/sPMR (18.4%) ($p < 0.001$)*, Post-operative VAS: 0.96 vs 1.94, $p = 0.01$ Mesh removal: 6.7%
Kohler et al. [30]	7.2/18.5, $p < 0.03$*	26,1/18, $p = 0.30$	1.56/2.02 (mean VAS) $p = 0{,}89$	N/A	Pain at 6 weeks: 1.61 vs 0.78, *$p = 0.02$ Time to final wound healing after SSI (weeks): 5 vs 8, $p = 0.03$* Trunk extension (elongation umbilicus-xiphoid in cm): 1.73 vs 2.40, $p = 0.009$
Muysoms et al. [25]	[0.0,6.0]/ [17.0,41.0], $p < 0.001$*	Wound: 1.8/5.1, $p > 0.05$ MeSH: 0	2/2, $p > 0.05$	3.6/0, $p > 0.05$	Pneumonia: 9% vs 26%, $p < 0.05$* Operative time: 211 vs 190 min., $p < 0.05$* Mesh removal: 1.8%
Pans et al. [20]	23/28.5, $p = 0.43$	3.5/2.8, $p > 0.05$	N/A	N/A	
Pizza et al. [52]	6/22, $p < 0.01$*	6/6, $p > 0.05$	0.24/0.22, (mean VAS)	4/6, $p > 0.05$	Re-operation: 4% vs 4%, $p > 0.05$

Table 2 continued

Study	IH incidence (PMR/PS) (%)	Infection (PMR/PS) (%)	Chronic pain (PMR/PS) (%)	Seroma (PMR/PS) (%)	Other results (PMR/PS)
Sarr et al. [13]	17.3/19.5, $p = 0.60$	Wound: 11.9/3.6, $p < 0.003$* MeSH: 0	17.3/10.8, $p = 0.08$	4.9/0.5, $p \leq 0.01$*	Operative time: 14 min extra in PMR Erythema: 13.5% vs 1.0%, $p \leq 0.001$*
Strzelczyk et al. [53]	0/21	N/A	N/A	14/11%	
Argudo et al. [54]	5.9/33.3, $p < 0.001$*	Wound: 26.3/17.9, $p = 0.13$ MeSH: 0%	N/A	N/A	Mesh removal: 0%
Argudo et al. [21]	10/43.9, $p < 0.001$*	N/A	N/A	Sign more in Mesh *	10.057€ vs 10.921€, $p < 0.001$
Curro et al. [27]	4.4/30, < 0.05*	2.2/6, $p > 0.05$	15.5/14, $p > 0.05$	N/A	
Kurmann et al. [55]	3.2/28.6, $p < 0.001$*	Wound: 60.3/61.9, $p = 0.603$	N/A	N/A	Mesh removal: 0%
Llaguna et al. [56]	2.2/17.7, $p < 0.01$*	9.09/1.61, $p = 0.07$	13.64/1.61, $p < 0.01$*	N/A	
Von Ahrens et al. [57]	7.7/16,5, $p > 0.05$	0/5.9	N/A	15/0	

* Significant result

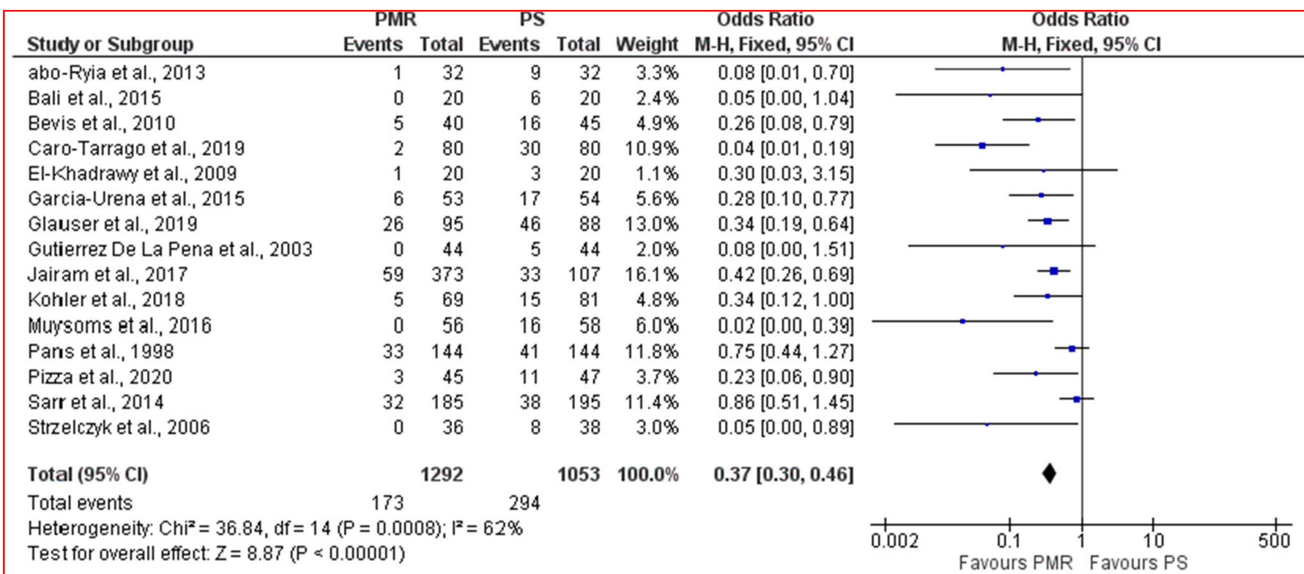

Fig. 2 Forest plot of the OR for IH incidence after laparotomy, based on RCT-studies

formation may however benefit QoL as well as reduce health care costs. In this systematic review, we analyzed the currently available literature, evaluating specific possible arguments for surgeons not to implement mesh prophylaxis after midline laparotomy.

Although 80% of the surgeons around the world use specific suturing techniques for hernia prevention, only 15% reported using prophylactic mesh. 11% of the surgeons are not familiar with the literature while 12% admit not to have the surgical knowledge for applying mesh insertion, neither onlay nor sublay positioning. Raising awareness and provide surgical videos are necessary as this should not be the reason not to apply a superior technique [12].

Table 3 Events, odds ratio (OR), risk ratio (RR) and risk difference (RD)

Meta-analysis	Events PMR vs PS (%)	OR	RR	RD
Hernia RCT	173/1292 (13.4) vs 294/1053 (27.9)	0.37 [0.30, 0.46]	0.46 [0.38, 0.55]	− 0,15[− 0.19, − 0.12]
Hernia Cohort	19/341 (5.6) vs 129/480 (26.9)	0.15 [0.09, 0.25]	0.20 [0.13, 0.32]	− 0.22 [− 0.27, − 0.17]
Infection RCT	120/1261 (9.5) vs 89/1006 (8.8)	1.00 [0.74, 1.35]	1.00 [0.77, 1.30]	− 0.00 [− 0.02, 0.02]
Infection Cohort	63/229 (27.5) vs 82/366 (22.4)	1.19 [0.76, 1.86]	1.10 [0.86, 1.40]	0.02 [− 0.04, 0.08]
Seroma RCT	104/1031 (10.1) vs 36/777 (4.6)	2.18 [1.45, 3.29]	2.00 [1.38, 2.90]	0.05 [0.02, 0.07]
Chronic pain RCT	44/412 (10.7) vs 29/416 (7.0)	1.68 [1.02, 2.76]	1.56 [1.02, 2.40]	0.04 [0.00, 0.08]

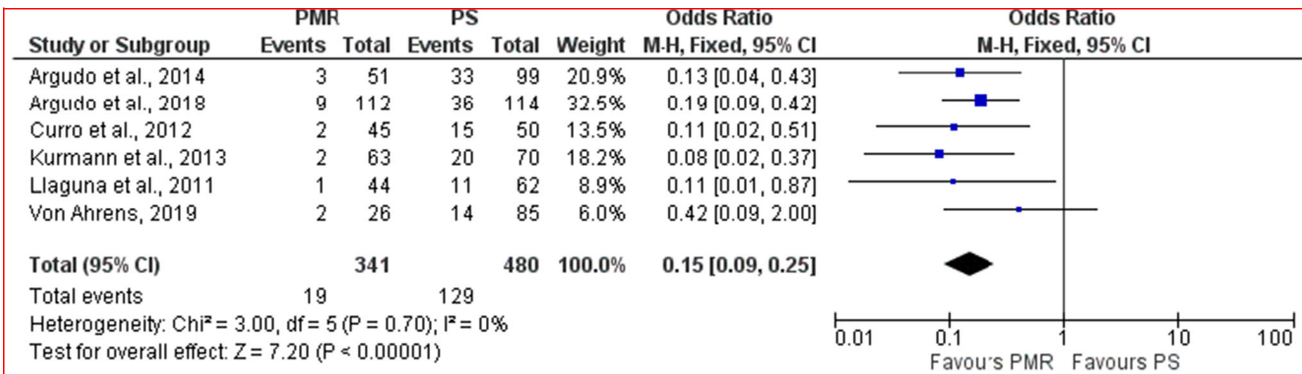

Fig. 3 Forest plot of the OR for IH incidence after laparotomy, based on cohort studies

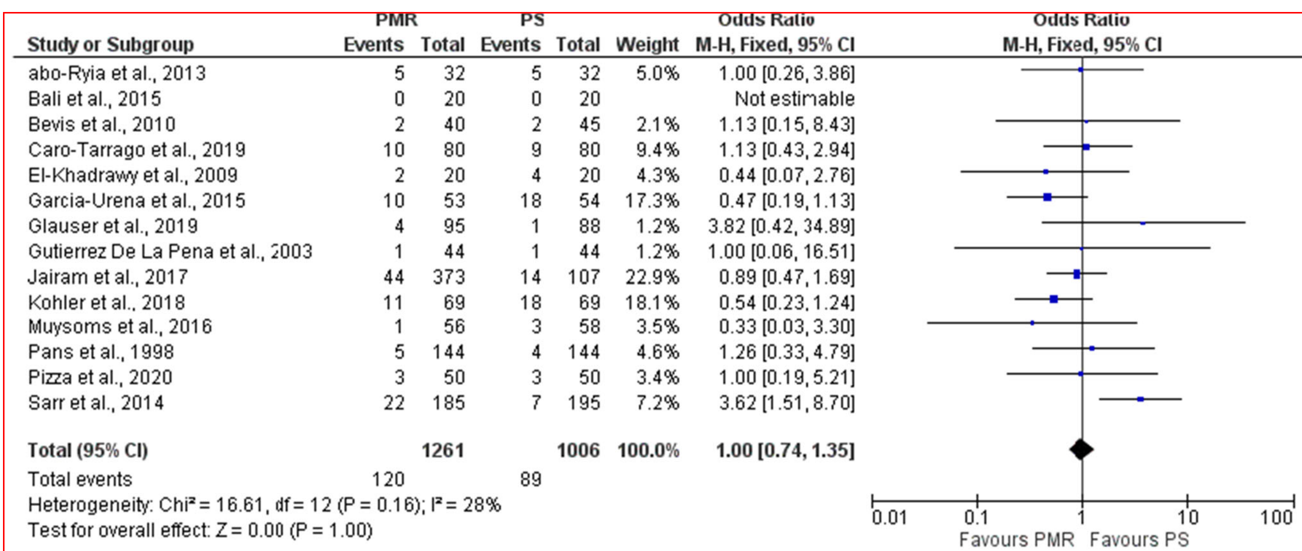

Fig. 4 Forest plot of the OR for post-operative infection (SSI and mesh), based on RCT-studies

During the survey by Fisher and colleagues, 23% of the surgeons are not convinced of the efficacy [12]. But PMR significantly reduces IH formation, as an odds ratio (OR) for IH incidence of 0.37 (95% CI = [0.30, 0.46] with RCTs and of 0.15 (95% CI = [0.09, 0.25]) in cohort studies was calculated. Encouraging results for intraperitoneal mesh reinforcement showed a 17% incisional hernia rate versus 39% in the primary closure group after 2 years' follow-up

Study or Subgroup	PMR Events	PMR Total	PS Events	PS Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Argudo et al., 2014	20	51	34	99	40.4%	1.23 [0.61, 2.48]
Curro et al., 2012	1	45	3	50	8.0%	0.36 [0.04, 3.55]
Kurmann et al., 2013	38	63	39	70	42.1%	1.21 [0.61, 2.41]
Llaguna et al., 2011	4	44	1	62	2.2%	6.10 [0.66, 56.58]
Von Ahrens, 2019	0	26	5	85	7.4%	0.28 [0.01, 5.16]
Total (95% CI)		**229**		**366**	**100.0%**	**1.19 [0.76, 1.86]**
Total events	63		82			

Heterogeneity: Chi² = 4.09, df = 4 (P = 0.39); I² = 2%
Test for overall effect: Z = 0.75 (P = 0.45)

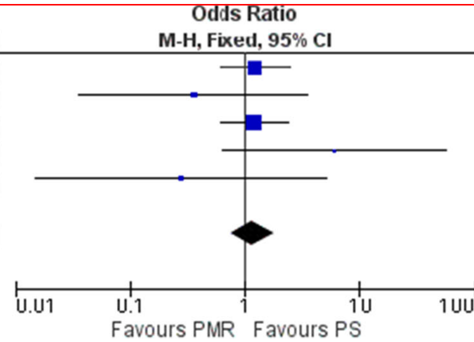

Fig. 5 Forest plot of the OR for post-operative infection (SSI and mesh), based on cohort studies

Study or Subgroup	PMR Events	PMR Total	PS Events	PS Total	Weight	Odds Ratio M-H, Fixed, 95% CI
abo-Ryia et al., 2013	6	32	5	32	12.1%	1.25 [0.34, 4.59]
Bali et al., 2015	2	20	1	20	2.7%	2.11 [0.18, 25.35]
Bevis et al., 2010	1	40	0	45	1.4%	3.46 [0.14, 87.26]
Caro-Tarrago et al., 2019	23	80	9	80	19.1%	3.18 [1.37, 7.42]
El-Khadrawy et al., 2009	4	20	3	20	7.1%	1.42 [0.27, 7.34]
Glauser et al., 2019	2	95	2	88	6.0%	0.92 [0.13, 6.71]
Gutierrez De La Pena et al., 2003	1	44	3	44	8.7%	0.32 [0.03, 3.18]
Jairam et al., 2017	47	373	5	107	20.2%	2.94 [1.14, 7.59]
Muysoms et al., 2016	2	56	0	58	1.4%	5.37 [0.25, 114.32]
Pizza et al., 2020	2	50	3	50	8.6%	0.65 [0.10, 4.09]
Sarr et al., 2014	9	185	1	195	2.8%	9.92 [1.24, 79.09]
Strzelczyk et al., 2006	5	36	4	38	10.0%	1.37 [0.34, 5.57]
Total (95% CI)		**1031**		**777**	**100.0%**	**2.18 [1.45, 3.29]**
Total events	104		36			

Heterogeneity: Chi² = 10.07, df = 11 (P = 0.52); I² = 0%
Test for overall effect: Z = 3.72 (P = 0.0002)

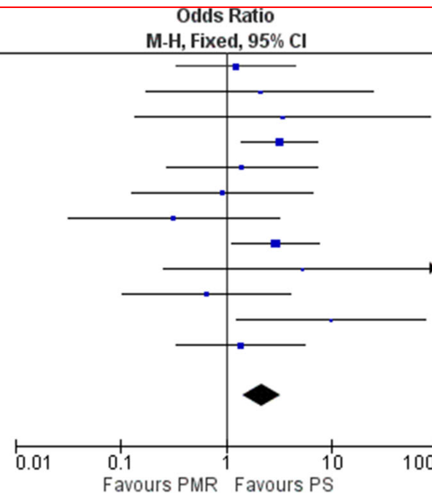

Fig. 6 Forest plot of the OR for post-operative seroma, based on RCT-studies

Study or Subgroup	PMR Events	PMR Total	PS Events	PS Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Caro-Tarrago et al., 2019	0	80	0	80		Not estimable
El-Khadrawy et al., 2009	3	20	0	20	1.7%	8.20 [0.40, 169.90]
Gutierrez De La Pena et al., 2003	2	50	0	50	2.0%	5.21 [0.24, 111.24]
Kohler et al., 2018	6	29	7	30	22.4%	0.86 [0.25, 2.94]
Muysoms et al., 2016	1	48	1	41	4.3%	0.85 [0.05, 14.05]
Sarr et al., 2014	32	185	21	195	69.5%	1.73 [0.96, 3.13]
Total (95% CI)		**412**		**416**	**100.0%**	**1.68 [1.02, 2.76]**
Total events	44		29			

Heterogeneity: Chi² = 2.95, df = 4 (P = 0.57); I² = 0%
Test for overall effect: Z = 2.03 (P = 0.04)

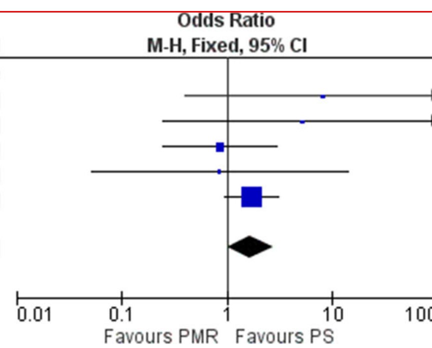

Fig. 7 Forest plot of the OR for chronic pain, based on RCT-studies

($P < 0.001$) [28, 29], while the PRIMA trial randomized 480 high-risk patients to 3 treatment arms: primary suture, onlay, and sublay [30]. At 2 years' follow-up, there was 33/107 (30%) IHs in the suture-only group, 25/188 (13%) in the onlay mesh-reinforcement group and 34/185 (18%) in the sublay-reinforcement group (onlay vs primary suture $P = 0.0016$; sublay vs primary suture $P = 0.05$).

In high-risk patients, like obese patients and patients with AAA, even a bigger decrease can be expected. According to Jairam et al. [7] and Argudo et al. [31], a BMI higher than 27 kg/m^2 or 29 kg/m^2, respectively, seems a good indication for PMR. Although the clinically heterogeneity is limited and a graphical evaluation of the forest plot shows that all studies favor PMR, there is a statistical heterogeneity between RCTs (I^2 = 62%). The heterogeneity originates from four studies specifically Sarr et al. [13], Caro-Tarrago et al. [24], Muysoms et al. [25], Pans et al. [20], but no specific reasons could be identified.

The European Hernia Society did not yet recommend PMR in their guidelines [32]. But since then many publications suggest the use of mesh to prevent IH after abdominal surgery. Three mesh locations have been studied to reinforce fascial closure of midline wounds. [33] Available evidence indicates that all 3 seem effective in reducing IH formation. A RCT by Jairam et al [8]. reported better IH prevention with onlay placement in comparison with sublay. Also the simplicity of the onlay procedure is an advantage. Data concerning intraperitoneal and inlay mesh reinforcement are scarce.

46.9% of the surgeons are concerned about mesh infection and other mesh-related complication. This seems actually to be the main reason not to implement prophylactic mesh use in their routine practice [12]. Looking at the outcome of this systematic review, the risk of SSI is equal with versus without PMR. If an infection occurs, a mesh removal is not always necessary. Two articles reported the necessity of mesh removal in 1.6% and 6.7%, while the other articles reported no mesh removals. Garcia-Urena et al. [34]. included both elective and emergency colorectal operations without hemodynamic instability of the patient during the operation. A total of 107 patients were included, with clinical and radiological follow-up for 24 months. There was no significant difference in surgical site infection between the suture-only group (33.3%) and the suture-plus-mesh group (18.9%).

Onlay and sublay mesh reinforcement show an increased risk of seroma formation, though this is not usually a significant clinical problem. A doubling of seroma rate to 10.4% is found when using mesh. Jairam et al. [8] reported a significant increase of seroma when the onlay approach is used in comparison with the sublay approach.

PMR also presented a slightly increased risk of chronic wound pain compared with primary suture [35]. An OR of 1.68 was found in this analysis, which was borderline significant. The risk increased from 7.0 to 10.7%. However, it has to be mentioned that Sarr et al. [13] was accountable for 69% of the weight in this analysis, showing chronic pain in 32 out of 185 patients after PMR using a bioprosthesis. Only two studies reporting chronic pain, used a sublay technique. These two studies show an OR of 2.93 (95% CI = [0.46, 18.67]) [25, 36]. The role of mesh fixation considering chronic pain remains unclear. Data on mesh fixation in PMR are scarce: only 2 retrospective studies show a safe implementation and possible reduction of chronic pain with fibrin sealant [37, 38].

Additional mesh costs and increased operating time might be another argument not to implement PMR in daily clinical practice. However, Fischer et al. [39] performed a cost-effectiveness analysis of PMR in high-risk patients with 719 included patients. A dominant incremental cost-effectiveness ratio (ICER) of $42,444/QALY was found. In a Monte Carlo sensitivity analysis, a proportion of 11.5% showed that PMR was dominant to primary suturing and a proportion of 36.2% showed that PMR lays under the $50,000/QALY threshold. This threshold might increase to $91,318 in Belgium, following the guidelines of the World Health Organization [40]. Argudo et al. [31] chose to implement mesh reinforcement in patients with a HERNIAscore higher than 7 (HERNIAscore = 4 × 1 (= laparotomy) + 3 × 0 (= no hand-assisted laparoscopy) + 1 × COPD + 1 × BMI > 25). The primary outcome was mean cost. They saw a significant reduction in total cost (10,057€ vs. 10,921€, $p < 0.001$) using an algorithm for patient selection, especially in obesity (10,210€ vs 13,588€, $p <$ 001), but not in low risk patients (9,226€ vs. 10,279€, $p = 0.323$). So PMR might be cost-efficient and can improve the quality of life, mainly in high-risk patients. 6.4% of the surgeons reported that mesh augmentation takes too long to perform [12]. Only 3 studies reported a slightly increased operation time of 10–20 min [9, 13, 25]. Despite the closing time is coffee time dogma, this might certainly not be an excuse for increased IH rates.

Fear for long-term sequellae of mesh implantation seems not valid either. Glauser et al. reported their experience using an intraperitoneal onlay mesh after more than 5 years of follow-up. Between the second and fifth year, there were no reported complications associated with the mesh [41].

Results of previous systematic reviews are similar. Jairam et al. [42] published their meta-analysis and trial sequential analysis including all studies until 1 January 2017. A significant reduction in incisional hernia rate was observed, specifically in high-risk patients. PMR was found to be safe, with no increase in SSI. Others also found a significant decrease in the incidence of IH [43–47], in some associated with a positive effect on QoL [43]. Sugrue et al. [48] summarized the available evidence in more than 2700 patients showing that besides an optimal laparotomy closure technique, preventive mesh placement should be considered in higher risk patients and if not, surgeons need to question why. Our review also has several limitations. No separate bias analyses were performed on the studies. In the included studies, there are differences in follow-up method and duration. A significant heterogeneity was found in the RCTs. The quality of the studies also varies, but low quality studies were excluded.

PMR can efficiently and safely prevent IH, especially in high-risk patients with a BMI over 29 kg/m^2 and with connective tissue disorders. This will increase QoL and is likely to be cost-efficient. Only an increase in seroma rate can be expected, while chronic pain seems slightly increased after mesh reinforcement. SSI and other complications are not increased using PMR. For now, a polypropylene, lightweight, large-pore mesh, in the onlay position is the best recommendation. It's important that both surgical techniques, new indications and long-term effects are further analyzed. The evidence for the use of PMR is overwhelming, but implementation in daily clinical practice remains limited. Instead of putting their patients at risk for incisional hernia formation and subsequent complications, surgeons should question their arguments why not to use PMR, specifically in high-risk patients.

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