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ORIGINAL ARTICLE

Retrospective Study

Different types of mechanical complications after surgical correction of adult spine deformity with osteotomy

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Author contributions: Barton C substantial contributions to conception and design of the study, acquisition of data, and drafting of the article; Noshchenko A provided statistical analysis and interpretation of the obtained results, drafting the article; Patel VV, Cain CMJ and Kleck C contributed equally to this work making critical revisions related to important intellectual content of the manuscript; Burger LE provided data quality control, critical revision of the manuscript and final approval of the version of the article to be published.

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Informed consent statement: Specific consent was not applicable due to the retrospective design of the study; personal data of the patients were not collected for the study.

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Abstract

AIM

To determine the incidence and risk factors for mechanical complications (MC) after surgical correction of adult spinal deformity (ASD) with osteotomy.

METHODS

A retrospective study was performed. Inclusion criteria: Surgical correction of ASD using osteotomy; male or female; > 20 years old; follow-up ⩾ 24 mo or revision. The MC of spine and spinal instrumentation were studied separately. Risk analysis included assessment of the association between more than 50 different characteristics (demographic, clinical, radiographic, and instrumentation) with different types of MC.

RESULTS

The medical records of 94 operations in 88 subjects were analyzed: Female (68%), mean age 58.6 (SD, 12.7) years. Cumulative incidence of MC at 2 year follow-up was 43.6%. Of these, 78% required revision ($P < 0.001$). The following characteristics had significant ($P \leqslant 0.05$) association with MC: (1) Preoperative: osteoporosis, smoking, previous spinal operation, sagittal vertical axis (SVA) > 100 mm, lumbar lordosis (LL) < 34°; (2) postoperative: SVA > 75 mm; operative correction: SVA > 75 mm, LL > 30°, thoracic kyphosis > 25°, and pelvic tilt > 9°; a fall; pseudarthrosis; and (3) device and surgical technique: use of previously implanted instrumentation; use of domino and/or parallel connectors; type of osteotomy (PSO *vs* SPO) if preoperative SVA < 100 mm; lumbar osteotomy location; *in-situ* rod contouring > 60°; and fixation to sacrum/pelvis.

CONCLUSION

Risk of MC after surgical correction of ASD is substantial. To decrease this risk over- and/or insufficient correction of the sagittal imbalance should be avoided.

Key words: Adult spinal deformity; Osteotomy; Risk factors; Mechanical complications

Core tip: The main study goal was evaluation of incidence and risk factors for different mechanical complications (MC) after surgical correction of adult spine deformity with osteotomy. Around half of patients experienced complications during two postoperative years; 78% of these cases required additional surgery. MC of spine occurred earlier and more often required revision than the MC of spinal instrumentation. The main risk factors for MC included severe preoperative sagittal imbalance, inadequate correction of the spinopelvic alignment, preoperative comorbidities (osteoporosis), postoperative events (falls), and features of the spinal instrumentation.

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INTRODUCTION

Surgical correction of adult spinal deformity (ASD) often requires one or more osteotomies such as a Smith-Petersen (SPO) and/or pedicle subtraction (PSO); SPO involves resection of the posterior column of the spine while PSO utilizes a resection of a triangular wedge through the pedicle and vertebral body[1,2]. In general a PSO can achieve significantly greater correction than a single SPO, and has been utilized for spinal deformities with severe sagittal imbalance, with relatively good clinical outcomes[3-10]. However, this method increases the risk of postoperative complications, which may result in revision surgeries[8-14]. The reported cumulative rate of revisions after surgical correction of ASD ranged from 28% at 24 mo follow-up[15] to 48% at 49 mo follow-up[11], with an increased cost in treatment. It was noted that the majority of these reoperations were related to mechanical complications (MC)[11,16]. Currently, there is no generally accepted definition of MC in spinal surgery. These have been described as failure of the fusion, spine or instrumentation. Therefore, the reported incidence of MC after surgical treatment in ASD is heterogeneous, and varies from 3.7% to 37%[10-12,17-24]. Published data concerning risk factors for MC in ASD corrected with an osteotomy are fragmented and suffer from several limitations. In particular, it was found that rate of postoperative symptomatic pseudarthrosis identified at 2-5 years after PSO was 10.5%. Patients with pseudarthrosis had significantly higher rates of previous fusion surgeries with pseudarthrosis, previous lumbar decompression, preoperative radiation of the spine/sacrum, and a preoperative history of inflammatory arthropathies/neurological disorders[25]. However, the level of corresponding risk was not evaluated. It was also noted that insufficient correction of spinal sagittal alignment with a PSO may be linked to pseudarthrosis and proximal junctional failure (PJF)[26]. However, the level of correction was defined by an integral index, making interpretation of the results difficult, and risk analysis was not performed. The reported incidence of symptomatic rod fracture (RF) after surgical correction of ASD with any osteotomy is cosistent: 5.3%[27], and 6.8%[14]; after a PSO it was higher: 15.8%[14] and 16.2%[27]. The following risk factors of RF were revealed ($P \leqslant 0.05$): Fusion construct crossing the thoracolumbar and lumbosacral junctions (OR = 9.1); maximum sagittal rod contour $\geqslant$ 60° (OR = 10.0); application of dominos and/or parallel connectors in the instrumentation constract (OR = 10.0); pseudarthrosis diagnosed at $\geqslant$ 1 year follow-up (OR = 28.9); and fixation to pelvis[27]. However, only a limited number of RF cases were included, which could cause an underestimation of the risks associated with other factors.

While the literature lacks clear evidence about the risk factors for MC after osteotomies, we expanded our literature search to MC after surgery for ASD (non-specific to osteotomy). This yielded several factors significantly ($P \leqslant 0.05$) associated with MC. In particular: The number of instrumented segments; fusion to the sacrum; and high preoperative pelvic tilt (PT), > 26°[11]. This was limited as MC were not specified, and were combined with neurological complications. In another study, MC after spinal fusion in ASD were classified as: (1) Proximal junctional complications including fracture of upper instrumented vertebra (UIV) and/or one level above (UIV + 1); and postoperative pseudarthrosis[16]. In this study the following

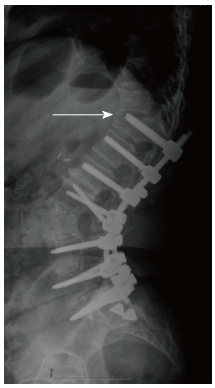


Figure 1 Example of radiographic findings of proximal junctional failure. Compression fracture of T11 proximal junctional failure (PJF) with screw pullout is shown by a black arrow. It was diagnosed at 1 mo follow-up after the surgical adult spine deformity correction using lumbar osteotomy and long thoracolumbar fusion surgery with fixation to sacrum. Before diagnosis of PJF, the patient experienced increased back pain limiting walking distance and increasing sagittal imbalance. The patient was revised with removal of the pedicle screws at T11 with extension of instrumentation to T9 two months after the index surgery.

risk factors were revealed: ⩾ 3 comorbidities, hazard ratio (HR) = 3.2; smoking, HR = 3.3; and preoperative sagittal imbalance with sagittal vertical axis (SVA) > 95 mm, HR = 2.7[16]. When compiling the data from multiple studies, the following preoperative spinopelvic measurements were identified as risk factors for PJF: SVA > 50 mm, OR = 2.5[28]; thoracic kyphosis (TK) > 30°, HR = 3.2[29-31]; and pelvic incidence (PI) > 55°[29,31]. Risk factors for PJF were also associated with postoperative overcorrection of the spinopelvic alignment, including: Postoperative SVA change[32], in particular, postoperative SVA < 50 mm[33]; change of TK > 10°[34], or > 30°, OR = 2.5[28]; and change of lumbar lordosis (LL) > 30°, OR = 4.8[28], HR = 2.4[31]. Risk factors for PJF associated with instrumentation and surgical technique included: Posterior spinal fusion[32], and fixation to the sacrum or pelvis, OR = 2.2[28,32,33]. Finally, risk of PJF was linked to the following demographic data: Male[8]; age > 55[35-37]; osteoporosis[32]; and increased body mass index (BMI)[35,36]. However, in some of the studies referenced above, the level of risk was not assessed properly. It is unclear how the revealed risk factors can be modified by the implementation of an osteotomy; whether there is a synergistic effect of different risk factors? If normal postoperative SVA < 50 mm is associated with risk of MC[28], what postoperative SVA or combination of factors is associated with less risk? The predictive value of the revealed risk factors was not defined.

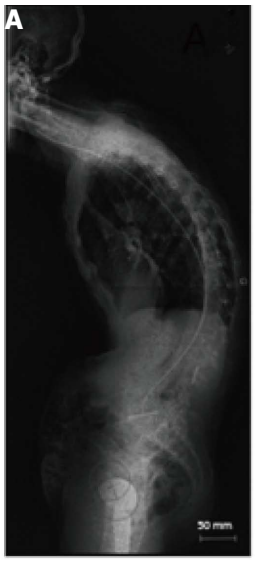
The purpose of this study was to evaluate the most clinically relevant MC seen after surgical correction of ASD with corrective osteotomies, taking into account the incidence, period of occurrence, association with additional surgeries, and assessment of risk factors associated with the MC and their predictive value.

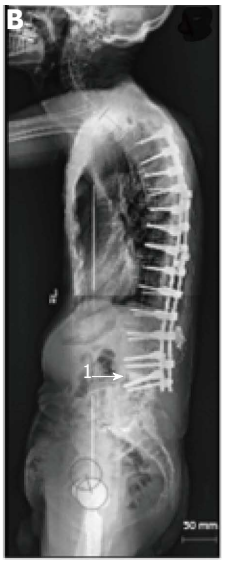
MATERIALS AND METHODS

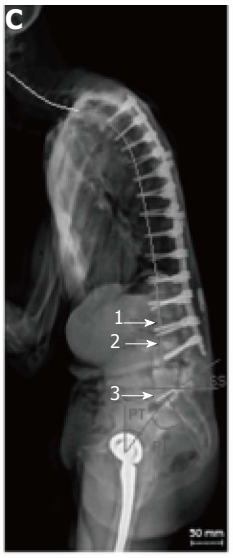
After institutional review board approval (COMIRB #14-1258), medical records and radiographic images were retrospectively identified in patients with ASD undergoing surgical correction with an instrumented spinal fusion including one or more osteotomies of the thoracic and/or lumbar spine. These operations were performed between 2007 and 2014 by 4 surgeons at a single institution. Inclusion criteria were used: (1) Demographics: Age > 20 years; gender, male and female; (2) diagnosis of ASD from any of the following etiologies: fixed sagittal imbalance, idiopathic or degenerative scoliosis, kyphosis or kyphoscoliosis, posttraumatic kyphosis, idiopathic or postoperative flat back syndrome, and ankylosing spondyloarthropathies; and (3) operation consisting of ⩾ 2 spinal posterior instrumented fusion levels (with or without interbody fusion) of the lumbar, or thoracic spine and having an osteotomy (PSO and/or SPO). All patients had to have follow-up not less than 2 years or undergone revision/reoperation prior to 2 year follow-up. Exclusion criteria consisted of: Malignancy, infection, congenital diseases, acute trauma, or latest follow-up < 2 year (unless revision surgery was performed at any postoperative time-point). If a patient had multiple SPOs during one operation, it was analyzed as one SPO procedure. If an operation included both SPOs and PSO, it was analyzed as one PSO procedure. The final decisions regarding inclusion/exclusion for each case was made by the project principal investigator (EB).

The following MC were taken into consideration: (1) MC of the spine: Vertebral fracture (VF): Single or multiple fractures of the vertebral body, vertebral endplate, and/or pedicle at any level(s) of the spine; PJF: Fracture and/or severe spondylolisthesis of the UIV and/or adjacent vertebra (UIV+1) (Figure 1); Distal segment degeneration/failure (DSF): Vertebral fracture and/or significant spondylolisthesis, collapse of the intervertebral disc(s) with or without herniation, stenosis with neurologic claudication at the lowest instrumented fused level (LIV) or caudally (Figure 2); and (2) MC of instrumentation: Screw loosening (SL): Failure of the bone-screw interface, including screw pull-out from the pedicle, sacrum, or ilium (Figure 3); RF: Fracture of one or both rods (Figure 4); iliac bolt connector failure (IBCF): loosening or fracture; disassociation of instrumentation (DI): Disconnection/loosening between any element(s) of the posterior fusion construct (Figure 5).

All types of MC were diagnosed radiographically and/or during revision surgery. The specific postoperative period when each MC was diagnosed was collected. The following characteristics were collected and assessed as potential risk factors: (1) Demographic: Age, gender, ethnicity, BMI, and smoking status at the time of the index operation; (2) Clinical: Primary diagnosis, indication for the index operation, osteoporosis, history of pseudarthrosis after previous operation (in cases of revision surgery); (3) Characteristics of the studied (index) operation: primary or revision, type of osteotomy (SPO/PSO), osteotomy location, number of posterior levels fused, transition segments of the spine crossed by posterior instrumentation, connection of new instrumentation to indwelling







PT 15°		PT 29°		PT 38°	
PI 27°		PI 50°		PI 68°	
LL -25°		LL -31°		LL -12°	
SS 12°		SS 21°		SS 30°	
PI-LL 5°		PI-LL 19°		PI-LL 56°	
SVA (C7) 92 mm		SVA (C7) 50 mm		SVA (C7) 156 mm	
TK 62°		TK 48°		TK 39°	
L4/L5 disc height		L4/L5 disc height		L4/L5 disc height	
Anterior	Posterior	Anterior	Posterior	Anterior	Posterior
9.2 mm	11.3 mm	9.6 mm	5.8 mm	3.2 mm	3.4 mm
L5/S1 disc height		L5/S1 disc height		L5/S1 disc height	
Anterior	Posterior	Anterior	Posterior	Anterior	Posterior
8.7 mm	5.7 mm	5.0 mm	1.7 mm	3.9 mm	1.3 mm
L5/S1 spondylolisthesis		L5/S1 spondylolisthesis		L5/S1 spondylolisthesis	
1 mm		2.5 mm		4.0 mm	

Figure 2 Example of distal segment degeneration/ failure. This event was observed after surgical correction of adult spine deformity in a patient (67 years old male) with idiopathic kyphoscoliosis complicated by degenerative disc disease and lumbar stenosis. A: Severe preoperative spinal kyphosis; B: Postoperative correction by T3-L4 posterior instrumented fusion with L3/L4 decompression, transforaminal interbody fusion by cage placement (1), and multilevel (T5-T11) Smith-Petersen osteotomy; C: Distal segment degeneration/ failure at 35 mo follow-up with deformation and/or fracture of L3 (1) subsidence of the interbody cage (2), collapse of L4/L5 and L5/S1 intervertebral discs with L5/S1 spondylolisthesis (3), loss of sagittal balance, and progression of proximal junctional kyphosis. Interestingly, these changes were accompanied by significant increase of pelvic incidence (PI) from 27o to 68o due to simultaneous increase of pelvic tilt (PT) and sacral slope which suggested that position of sacrum relatively to pelvis changed after surgery. Likely, this is the result of displacement in the sacroiliac joints. This finding contravenes the concept concerning postoperative stability of PI.

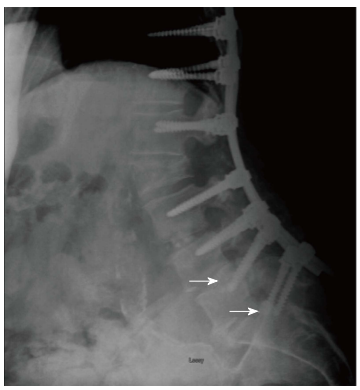


Figure 3 An example of radiographic findings of screw pullout/loosening. Screw pullout is shown by black arrows at L5 and S1 bilaterally identified at the 6 mo follow-up visit after surgical correction of adult spine deformity with osteotomy. Pseudarthrosis was diagnosed later at 12 mo post-operative. The patient experienced increasing low back pain and "popping" with movement. A revision operation was performed at 12 mo follow-up to revise the fusion and re-instrument, including placement of iliac bolts.

hardware, cement use, use of anterior supplemental fixation, fixation to the sacrum, fixation to the pelvis; (4) Characteristics of the instrumentation: Type of screws (polyaxial/monoaxial), screw manufacturer, type of rods (precontoured by manufacturer/no), rod material, thickness and shape of rods, greatest angle of rod contouring, manufacturer of rods, method of the rod contouring, number of crosslinks, number of domino and/or parallel connectors, use of bone morphogenetic protein (BMP); (5) Radiographic characteristics of spinopelvic alignment in standard preoperative and postoperative (1^{st}-4^{th} week after operation) images: SVA, LL, TK, PT, pelvic incidence (PI), PI-LL mismatch with discrete and absolute differences between postoperative and preoperative values of each spinopelvic parameter; and (6) Postoperative events: Fall after operation, but before diagnosis of MC, and postoperative pseudarthrosis (nonunion at the fused site(s) confirmed radiographically (plane radiography or computed tomography) or during revision at more than 1 year follow-

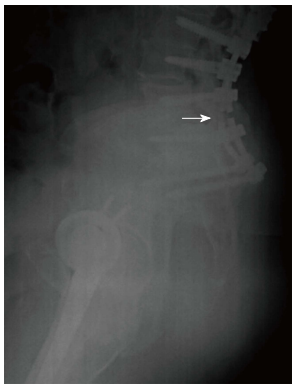


Figure 4 An example of radiographic findings of rod fracture. Bilateral L5-S1 rod fractures are shown by black arrow; they were diagnosed consequently at 12 and 20 mo follow-up after surgical correction of adult spine deformity, and accompanied with L5-S1 pseudo-arthrosis. The pseudo-arthrosis at L5-S1 was diagnosed simultaneously with the second rod fracture at 20 mo follow-up. The patient experienced increasing low back pain and sagittal imbalance. A revision operation was performed at 21 mo follow-up with revision of the fusion and an osteotomy to correct residual sagittal imbalance.

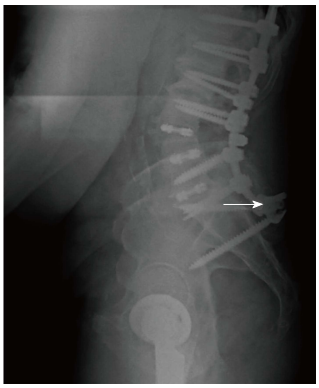


Figure 5 An example of radiographic findings of disassociation of instrumentation. Uncoupling of the rod from the iliac bolts disassociation of instrumentation is shown by black arrow; it was diagnosed at 4 mo follow-up after surgical correction of adult spine deformity. The patient experienced ongoing low back pain. A revision operation was performed with replacement of iliac screws and connectors. Intraoperatively, it was noted that the right pelvic screw cap had disengaged.

ups) Osteoporosis/osteopenia information was obtained from the patients' medical records by analyzing the results of dual energy X-ray absorptiometry or ultrasound evaluation.

Clinical and demographic data were extracted from the medical records by an experienced researcher (CB) under control of the project PI (EB). Spinopelvic parameters were defined by retrospective analysis of radiographic images using Surgimap surgical planning software (Nemaris Inc, New York, NY, United States) by a trained researcher (CB). Ten percent of the performed measurements were additionally evaluated by the PI (EB) to assess correspondence. Correspondence between these two measurements was assessed by the Kappa test[38]. Measurements were regarded identical, if deviation between them did not exceed 10% of the smaller value. The studied spinopelvic parameters were defined using currently accepted standards of measurement as outlined in previous studies[39,40]. If the quality of a radiographic image did not allow accurate assessment of a studied index, this index was excluded from analysis. Decisions concerning the exclusion were made by the project PI (EB) after discussion with Musculoskeletal Radiologists. All these exclusions were then taken into consideration as a potential source of bias.

The collected data were entered in to the electronic data base for further analysis. Data quality control was performed by 2 experts (EB and AN), and disagreements were resolved by discussion.

Statistical analysis

Following indices were applied to characterize the studied population: Quantitative characteristics were analyzed using number of observations, mean, standard deviation, median, minimum and maximum values[38]. Percentiles were applied for better description of distribution of spinopelvic characteristics before and after operation, and also difference between postoperative *vs* preoperative values (level of correction)[38,41]. Categorical characteristics were analyzed using percentage[38].

Cumulative number and incidence rate for each of MC for the studied postoperative period was calculated as a rate (0-1) or percentage with 95% confidence limits (95%CI)[41]. To define the postoperative period with maximum likelihood of occurrence, distribution of latent periods (time between the index operation and diagnosis of MC) were analyzed using percentiles[41]. Risk of postoperative revision/reoperation associated with each type of MC was defined by OR with 95%CI[41]. The *P*-value was defined by the χ^2-test[41]; if the number of studied events in any of the analyzed subgroups was small ($\leqslant$ 5), the Fisher-exact test (F) was applied[41]. Analysis of risk factors associated with MC was performed in a few stages. Initially, there were revealed factors that have statistically significant ($P \leqslant 0.05$) association with any type of MC. This analysis was performed using the logistic regression[38]. Then, quantitative characteristics that showed such association were categorized to define an exact range with the most significant risk of MC. The level of risk was assessed by OR (95%CI), and *P*-value was defined by the χ^2 or the Fisher exact tests[41]. Categorical indices were analyzed to identify a category having the most significant association with the MC. The level of risk was also assessed by OR (95%CI), and *P*-value by the χ^2 or the Fisher exact tests[41]. Grouping analysis was applied to reveal risk factors that are general for all or a few types of MC; in particular, those that are mainly associated with MC of the spine, and those that are mainly linked with MC of spinal instrumentation. Impact of confounders and combinations of different risk factors was defined by stratification, if it was applicable due to the number of cases[38]. Multiple regression analysis was applied to define prognostic capability of an integrative approach when a few risk factors having significant association with MC are taken into consideration. The JMP®7.0.1 (SAS

Table 1 Main demographic and clinical characteristics of the studied case series (patients who underwent surgical correction of adult spine deformity with osteotomy, *n* = 94)

Demographic characteristic	Subgroup (if applicable)	Measure units	Statistical characteristics	Value
Age	NA	Years	*n*	94
			Median	59.5
			Mean	58.6
			SD	12.7
			Min	23
			Max	82
Gender	Male	Subjects	Number (%)	30 (32)
	Female		Number (%)	64 (68)
Body mass index	NA	Conventional units	Number	79
			Median	26.6
			Mean	27.2
			SD	5.6
			Min	16.2
			Max	43.5
Primary diagnosis	Degenerative scoliosis	Subjects	Number (%)	9 (9.6)
	Idiopathic scoliosis		Number (%)	29 (31.1)
	Degenerative kyphosis		Number (%)	13 (13.9)
	Mixed and other adult spine deformities		Number (%)	43 (45.4)
Smoking status	Never	Subjects	Number (%)	38 (40.4)
	Former		Number (%)	37 (39.4)
	Current		Number (%)	14 (14.9)
	Not specified		Number (%)	5 (5.3)
Ethnicity	Caucasians	Subjects	Number (%)	82 (87.2)
	Hispanic		Number (%)	7 (7.4)
	Not specified		Number (%)	5 (5.3)
Osteoporotic status	Osteoporosis or osteopenia	Subjects	Number (%)	29 (30.3)

NA: Not applicable; SD: Standard deviation; Min: Minimum value; Max: Maximum value.

Institute Inc., United States; www.jmp.com) statistical program was used for analysis. The next stage of analysis included assessment of predictive values for each revealed risk factor. The predictive values included sensitivity (Sn), specificity (Sp), positive (+PV) and negative (-PV) predictive values[38]. There was applied following definition for each predictive value taking into consideration context of this study: Sn is the probability of risk factor presence if the MC has been diagnosed during the studied follow-up period; Sp is the probability of risk factor absence if the MC has been not diagnosed during the studied follow-up period; +PV is the probability of diagnosed MC during the studied follow-up period if the risk factor is present; -PV is the probability of absence of diagnosed MC during the studied follow-up period if the risk factor is absent. The Bayesian method was used to generalize the obtained results with previous findings, if it was applicable due to the quality of the previously published data. The previously published data were used as prior odds combining of which with the result of current study provided posterior odds (PO) which combined effects of the previous and the current data[42,43]. If the PO was $\geqslant 5$ or $\leqslant 0.2$, it was considered as a sufficient level of evidence of the generalized effect[42,43]. The statistical analysis was performed by statistician experienced in analysis of biomedical data who is a coauthor this publication (AN).

RESULTS

Initially, 118 patients who underwent 130 osteotomies were identified. Thirty patients and 36 corresponding operations were excluded due to < 2 year postoperative follow-up. Eighty-eight patients who had 94 operations were included; 6 of 88 patients had 2 operations, each was analyzed as a separate case. In total, 94 cases were analyzed. Mean follow-up was 30 mo.

The demographic characteristics of the included cases were: Female 68%, male 32%; mean age, 58.6 (SD, 12.7); mean BMI, 26.6 (SD, 5.6); smoking at the time of operation, 14.9%; ethnicity: Caucasians 87.2%, Hispanic 7.4, other 5.3% (Table 1).

The primary diagnosis included: Degenerative scoliosis and/or kyphosis, 23.5%; idiopathic scoliosis, 31.1%; combination of different etiologies of adult spine deformity, 45.4%. Concomitant osteoporosis or osteopenia: 30.3% (Table 1).

The characteristic of the studied (index) operations included: Primary, 21%; revision, 79%; number of levels fused: median 8, minimum 2 and maximum 17; type of osteotomy: SPO, 46%; PSO, 54%; osteotomy location: Lumbar, 62%; thoracic, 21%, thoracolumbar junction, 14%, and sacrum, 3%; transitional segments crossed by instrumentation: cervicothoracic, 2%; thoracolumbar, 26%; lumbosacral, 14%; thoracolumbar and lumbosacral, 51%; fixation to sacrum, 40%; fixation to pelvis, 23%; use of anterior fusion, 38%; number of anterior levels fused: Median, 2; minimum 2 and maximum 6; supplemental anterior fixation, 66%; cement use, 25%; BMP use, 52%; use of individually precontoured posterior rods, 34%; connecting of new

Table 2 Main characteristics of the index operation (surgical correction of adult spinal deformity with posterior instrumentation and osteotomy, *n* = 94)

Characteristics of operation	Subgroup (if applicable)	Measure units	Statistical characteristic	Value
Index operation	Primary	Subjects	Number (%)	20 (21)
	Reoperation		Number (%)	74 (79)
Number of fused levels	NA	Number	Median	8
			Min; max	2; 17
Type of osteotomy	PSO	Subjects	Number (%)	51 (54)
	SPO		Number (%)	43 (46)
Osteotomy location	Lumbar	Subjects	Number (%)	58 (62)
	Thoracic		Number (%)	20 (21)
	Thoracolumbar junction		Number (%)	13 (14)
	Sacrum		Number (%)	3 (3)
Inter-level junctions crossing by instrumentation	Cervicothoracic	Subjects	Number (%)	2 (2)
	Thoracolumbar		Number (%)	24 (26)
	Lumbosacral		Number (%)	13 (14)
	Thoracolumbar and lumbosacral		Number (%)	48 (51)
	No		Number (%)	7 (7)
Fixation to sacrum (not pelvis)	NA	Subjects	Number (%)	38 (40)
Fixation to sacrum and/or pelvis	NA	Subjects	Number (%)	59 (63)
Use of anterior fusion	NA	Subjects	Number (%)	36 (38)
Number of anterior levels fused	NA	Subjects	Median	2
			Min; max	1; 6
Supplemental anterior support/fixation by implant or instrumentation	NA	Subjects	Number (%)	62 (66)
Use of cement	NA	Subjects	Number (%)	23 (25)
Use of bone morphogenetic protein	NA	Subjects	Number (%)	49 (52)
Use of individually precontoured posterior rods	Precontoured	Subjects	Number (%)	32 (34)
	In situ contouring	Subjects	Number (%)	62 (66)
Connecting to previously implanted instrumentation	NA	Subjects	Number (%)	16 (17)
Use of Domino and/or parallel connectors	2	Subjects	Number (%)	2 (2)
	1		Number (%)	11 (12)
	0		Number (%)	81 (86)

NA: Not applicable; SD: Standard deviation; PSO: Pedicle subtraction osteotomy; SPO: Smith-Peterson.

instrumentation to previously implanted, 17%; use of domino and/or parallel connectors, 14% (Table 2).

The number of high quality images adequate for obtaining spinopelvic parameters was limited, but was enough to reach statistically significant results. Two independent evaluations of the studied radiographic indices showed good agreement by the Kappa test, 0.85 (SE, 0.09), $P = 0.08$.

Preoperative and postoperative characteristics of sagittal spinopelvic alignment were highly heterogeneous having distribution close to the normal (bell shaped curve) (Table 3). In particular, preoperative SVA ranged from 0 to 203 mm; 70% of patients had anterior sagittal imbalance (SVA > 50 mm, Table 3). After operative treatment the mean SVA decreased from 73.9 mm to 41.7 mm ($P < 0.001$) with the percentage of patients with the sagittal imbalance decreasing to 35%. However, variability remained high with values ranging from -66 mm to 167 mm. The absolute difference between postoperative and preoperative values ranged from 0 to 182 mm (Table 3).

Preoperative LL ranged from 4° to 99° with mean value 34.4°. After surgical treatment the mean value increased to 51.3° ($P < 0.001$), but variability remained high (Table 3). Absolute difference between postoperative and preoperative LL values varied from 1° to 50° (Table 3).

The mean preoperative TK was 39.4°, and extreme values ranged from -3° to 109°. While the mean value did not change significantly after operative treatment (41.9°), the absolute difference between postoperative and preoperative values varied from 0° to 41° with the mean value 12° suggesting significant ($P < 0.001$) reciprocal postoperative change (Table 3).

Preoperative PT ranged from 8° to 40° with a mean value of 27.8°. After surgery the mean decreased to 20.2 ($P < 0.001$), but variability remained high with extreme values from -4° to 51°. The absolute difference between postoperative and preoperative values ranged from 0° to 29° with a mean of 9.9° (Table 3).

Preoperative PI-LL ranged from -43° to 66° with the mean 20.9°. The mean decreased postoperatively to 3.8° ($P < 0.001$), but the range remained approximately the same. The absolute difference between postoperative and preoperative values ranged from 0° to 48° with the mean, 19.2° (Table 3).

A fall after surgery was observed in 15% (95%CI: 11.3; 18.7) of cases. Postoperative pseudoarthrosis was revealed in 10.6% (95%CI: 7.4; 13.6) of cases. One MC had 27.6% (95%CI: 23.0; 32.2), and multiple MC (from 2 to 4) had 16% (95%CI: 12.2; 19.8) of the patients.

Table 3 Characteristics of sagittal spinopelvic alignment before and after index operation, and level of perioperative change

Spinopelvic characteristic, units	Subgroup	*n*	Characteristics of distribution								
			Percentiles							Mean	SD
			Min	10	25	50	75	90	Max		
Sagittal vertical axis, mm	Preop	94	0	15	33	74	105	128	203	73.9	42.4
	Postop	61	-66	0.2	14	40	60	94	167	41.7	38.4
	Postop-Preop	61	73	34	-5	-30	-59	-96	-182	-33.1	47.8
	Postop-Preop (abs)	61	0	10	20	38	60	96	182	46	35.7
Lumbar lordosis, L1-S1, degree	Preop	77	4	8	19	36	45	56	99	34.4	19.4
	Postop	90	3	32	43	52	61	71	97	51.3	16.6
	Postop-Preop	74	-37	-6	4	16	30	38	50	16.1	17.4
	Postop-Preop (abs)	74	1	3	9	17	31	37	50	19.7	13.2
Thoracic kyphosis, T1-T12, degree	Preop	64	-3	11	23	39	54	64	109	39.4	21.9
	Postop	81	9	18	32	44	51	58	75	41.9	14.7
	Postop-Preop	62	-41	-19	-10	1	13	25	34	1.6	15.9
	Postop-Preop (abs)	62	0	1	2	12	18	29	41	12	10.3
Pelvic tilt, degree	Preop	68	8	13	19	27	35	43	48	27.8	10.4
	Postop	78	-4	9	13	20	27	33	51	20.2	9.7
	Postop-Preop	61	10	5	-2	-8	-15	-19	-29	-7.9	9.1
	Postop-Preop (abs)	61	0	2	5	8	15	19	29	9.9	6.7
Pelvic incidence – lumbar lordosis mismatch, degree	Preop	68	-43	-10	9	23	37	47	66	20.9	21.6
	Postop	78	-41	-17	-7	2	13	28	41	3.8	15.6
	Postop-Preop	61	25	4	-2	-18	-31	-37	-48	-16.2	16.6
	Postop-Preop (abs)	62	0	3	9	18	31	37	48	19.2	13.2

n: Number of measured cases; SD: Standard deviation; SEM: Standard error of the mean; Postop-preop: Difference between postoperative and preoperative values; Postop-preop(abs): Difference between postoperative and preoperative characteristics in absolute value.

Table 4 Undesirable postoperative events and additional treatment after surgical correction of adult spinal deformity with osteotomy (*n* = 94)

Index	Number of cases	Rate, % (95%CI: min; max)
Fall after operation before mechanical complication(s)	14	15% (11.3; 18.7)
Postoperative pseudarthrosis	10	10.6% (7.4; 13.6)
Cases with 1 mechanical complication	26	27.6% (23.0; 32.2)
Cases with a few (2-4) mechanical complications	15	16.0% (12.2; 19.8)
Additional surgical treatment (revision/reoperation)	40	42.5% (37.4; 47.6)
Additional conservative treatment	14	15.0% (11.3; 18.7)

Additional postoperative treatment was required in 57.5% of cases, including 42.5% (95%CI: 37.4; 47.6) requiring revision surgery, and 15% (95%CI: 11.3; 18.7) conservative treatment in only (Table 4).

The total incidence of cases with MC was 43.6% (95%CI: 33.4; 53.8%). MC of the spine occurred in 25.5% (95%CI: 16.5; 34.5); and MC of the instrumentation in 25.5% (95%CI: 16.5; 34.5, Table 5). Cases with MC of the spine included: VF in 20.2% (95%CI: 12.0; 28.4), PJF in 11.7% (95%CI: 5.2; 18.2), and DSF in 6.4% (95.5CI: 1.4; 11.4%, Table 5). Cases with MC of the instrumentation included: SL in 18.1% (95%CI: 14.1; 22.1), fracture of the screw in 2.1% (95%CI: 0; 4.9), RF in 7.4% (95%CI: 4.7; 10.1), IBCF in 4.3% (95%CI: 2.2; 6.5), and DI in 7.4% (95%CI: 4.7; 10.1) (Figure 6 and Table 5).

An association between MC and secondary surgical treatment was strong, OR = 20 (95%CI: 6.9; 57.4, $P < 0.001$) with 78% of cases of MC (32 of 41) leading to revision surgery. This association was the most significant ($P < 0.04$) in cases with MC of the spine, in particular: VF, PJF and DSF. It was also significant in MC of the instrumentation such as: SL and DI (Table 5).

Majority of MC (70%) were diagnosed during the 1st postoperative year (Figure 7). The shortest latent period had PJF, VF, SL (specifically screw fracture), and DI ($\geqslant$ 70% of these cases was revealed during 1st year). Longer latent periods (> 1 year in majority of cases) were seen in MC such as DSF, SL, RF, IBCF (Figure 7).

The following factors had significant association with MC (all types): Preoperative SVA > 110 mm, OR = 4.5 (95%CI: 1.3; 15.4), $P = 0.011$; postoperative SVA > 74 mm, OR = 5.4 (95%CI: 1.4; 21.1), $P = 0.014$; preoperative LL < 20°, OR = 5.5 (95%CI: 1.8; 16.9), $P = 0.002$; postoperative change of LL > 34°, OR = 4.7 (95%CI: 1.2; 18.0), $P = 0.028$; postoperative change of PI-LL > 34°, OR = 6.4 (95%CI: 1.2; 33.2), $P = 0.033$; type of osteotomy, SPO *vs* PSO, OR = 0.42 (95%CI: 0.18; 1.0), $P = 0.045$; fixation to sacrum with or without fixation to pelvic after PSO if number of fused

Table 5 Association of different types of mechanical complications with postoperative revision/reoperation after surgical correction of adult spinal deformity with osteotomy (n^1 = 94)

Mechanical complication	n^1	Association with revision/reoperation after index operation		
		n^2	OR (95%CI)	*P* value
Total (failure of spine and/or instrumentation)	41	32	20.0 (6.9; 57.4)	< 0.0001
Failure of spine (total)	24	21	18.8 (5.0; 70.3)	< 0.0001
Vertebral fracture (total)	19	17	19.2 (4.1; 90.1)	< 0.0001
PJF	11	11	> 19.0	< 0.0001
DSF	6	5	7.6 (0.8; 67.6)	0.033
Instrumentation failure (total)	24	18	6.6 (2.3; 18.8)	0.001
Screw loose	17	12	4.2 (1.3;13.2)	0.014
Screw fracture	2	2	NA	0.161
Rod fracture	7	4	1.9 (0.4; 8.9)	0.453
Iliac bolt connector (loose and/or fracture)	4	3	5.7 (0.6; 53.4)	0.308
Disconnection of instrumentation	7	6	9.4 (1.1; 81.1)	0.022

n^1: Number of cases with exact type(s) of mechanical complication; n^2: Number of cases required revision and/or reoperation after index operation; OR: Odds ratio; 95%CI: 95% Confidence limits; PJF: Proximal junctional failure; DSF: Distal segment degeneration/failure; NA: Not applicable.

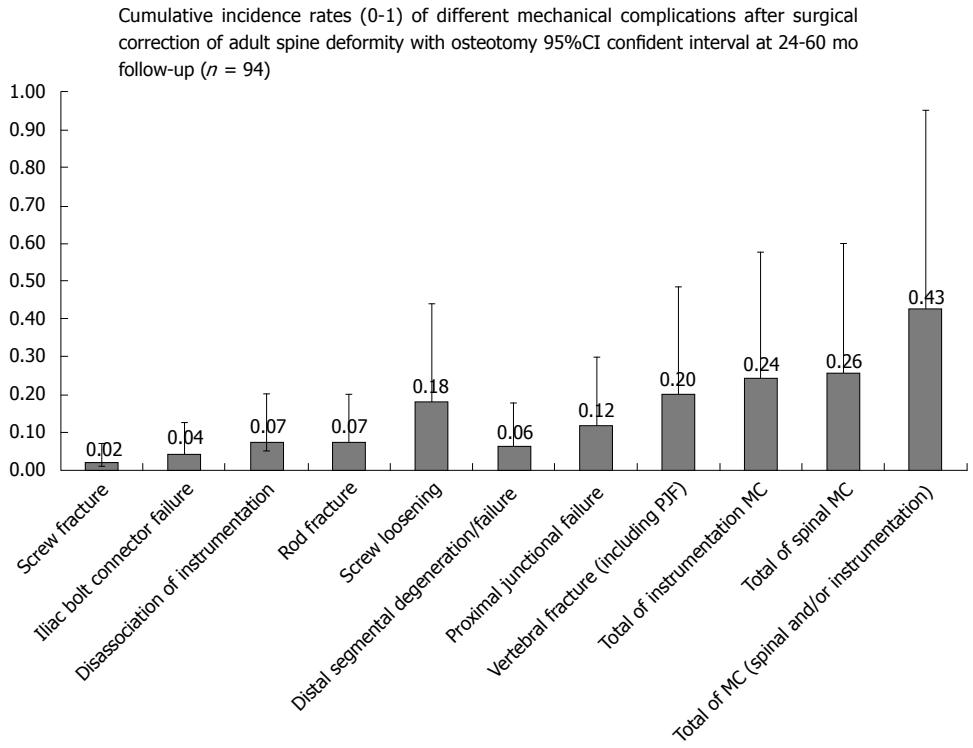


Figure 6 Cumulative incidence rates of different mechanical complications after surgical correction of adult spine deformity with osteotomy at long term postoperative follow-up; the error bars show 95%CI. PJF: Proximal junctional failure; MC: Mechanical complications.

levels > 4, OR = 3.6 (95%CI: 0.92; 13.9), *P* = 0.056; postoperative pseudarthrosis, OR = 14.6 (95%CI: 1.8; 120.9), *P* = 0.002 (Table 6). However, in spite of statistical significance, prediction capacity of these factors was limited, in particular, majority of them had low Sn (< 40%) (Table 6). To take into consideration all factors listed above, an integral index was obtained by multiple regression analysis using equation (1) described below. With this equation risk of MC ranged from 0 to 1. Analysis showed that the index values ⩾ 0.46 have the highest association with MC (OR = 31.7, 95%CI: 6.7; 149.3, *P* < 0.0001, Table 6). Predictive capacity of this integral index was in general higher than that of single characteristics, but did not exceed moderate level: Sn, 79%; Sp, 89%; +PV, 86%, and -PV, 83%.

$$y = 0.84 + X_1 + X_2 + X_3 + X_4 + X_5 + X_6 + X_7 + X_8 + X_9 \quad (1)$$

Where: y is risk of MC ranged from 0 to 1; X_1 is preoperative LL: < 20° match to 0.22, and ⩾ 20° match to (-0.22); X_2 is fall after surgery, but before MC: "yes", match to 0.15, and "no", match to (-0.15); X_3 is fixation to sacrum or pelvic: "yes", match to 0.07, and "no", match to (-0.07); X_4 is preoperative SVA: ⩾ 110 mm match to 0.04, and < 110 mm match to (-0.04); X_5 is

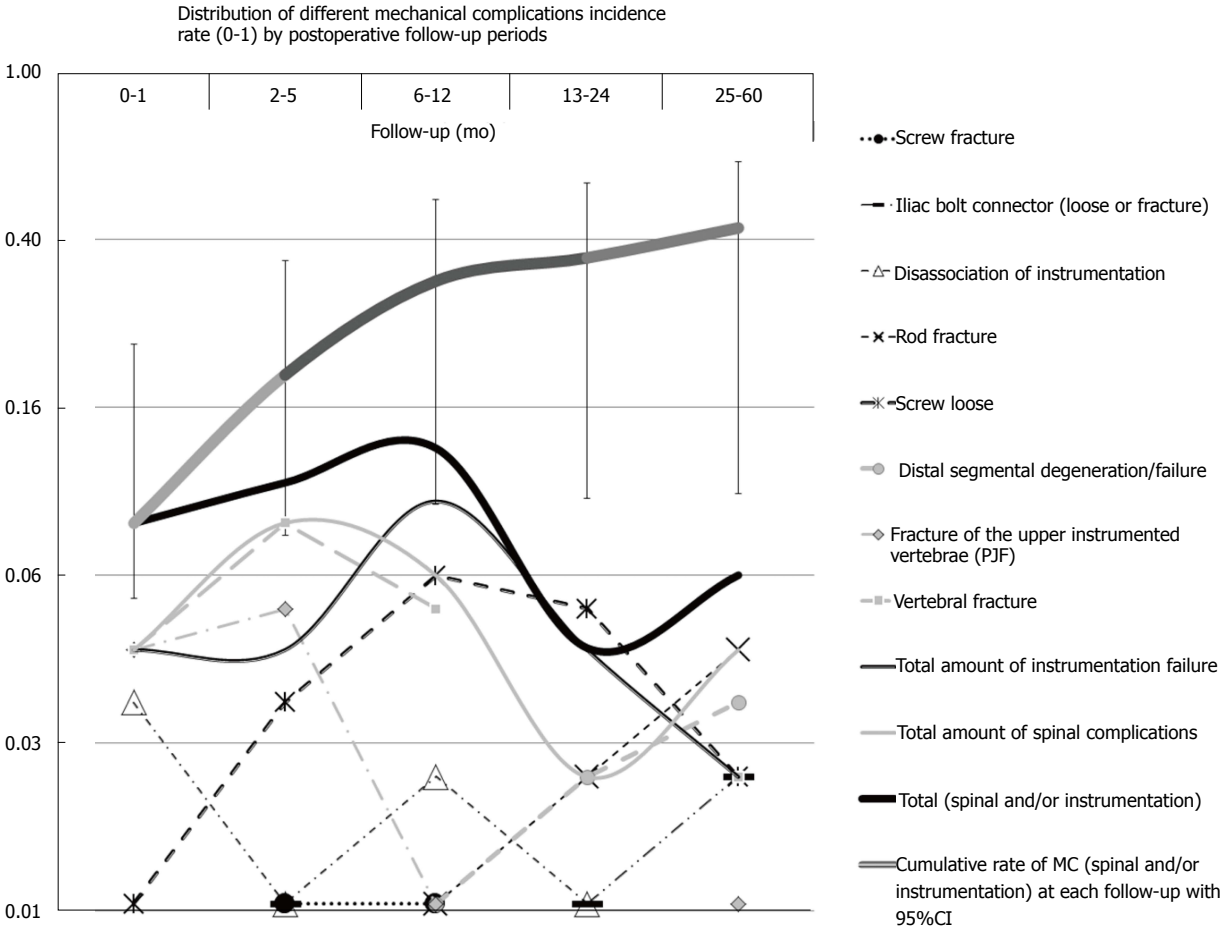


Figure 7 Distribution of different types of mechanical complications after surgical correction of adult spine deformity with osteotomy by different periods of long-term postoperative follow-up; the error bars show 95%CI. MC: Mechanical complications.

Table 6 Risk factors for mechanical complications (all types: Failure of spine and/or instrumentation) after surgical correction of adult spine deformity with osteotomy

Risk factor(s)	OR (95%CI: min; max)	*P* value	Predictive values			
			Sn	Sp	+PV	-PV
Preoperative SVA > 110 mm	4.5 (1.3; 15.4)	0.011	0.27	0.92	0.73	0.62
Postoperative SVA > 75 mm	5.4 (1.4; 21.1)	0.014	0.24	0.94	0.77	0.62
Preoperative LL< 20°	5.5 (1.8; 16.9)	0.002	0.37	0.91	0.75	0.65
Postoperative change of LL > 34° (absolute values)	4.7 (1.2; 18.0)	0.028	0.22	0.94	0.75	0.61
Postoperative change of PI-LL > 34° (absolute values)	6.4 (1.2; 33.2)	0.033	0.29	0.94	0.80	0.62
Type of osteotomy SPO *vs* PSO	0.42 (0.18; 1.0)	0.045	0.34	0.45	0.33	0.47
Fall after operation before mechanical complication	6.1 (1.6; 23.7)	0.007	0.27	0.94	0.79	0.63
Fixation to sacrum or pelvic if number of fused levels > 4	2.4 (0.9; 6.4)	0.068	0.74	0.46	0.53	0.68
Fixation to sacrum or pelvic if number of fused levels > 4 with PSO	3.6 (0.92; 13.9)	0.053	0.78	0.50	0.67	0.64
Postoperative pseudarthrosis	14.6 (1.8; 120.9)	0.002	0.22	0.98	0.90	0.62
Integral index based on parameters presented above by results of multiple regression modeling (1) ⩾ 0.46	31.7 (6.7; 149.3)	< 0.001	0.79	0.89	0.86	0.83

SVA: Sagittal vertical axis; LL: Lumbar lordosis; PI-LL: Pelvic incidence (PI) - lumbar lordosis (LL) mismatch; PSO: Pedicle subtraction osteotomy; SPO: Smith-Peterson osteotomy; OR: Odds ratio; 95%CI: min; max: 95% confidence limits, maximum and minimum values; Sn: Sensitivity; Sp: Specificity; +PV: Positive predictive value; -PV: Negative predictive value.

postoperative SVA: ⩾ 75 mm match to 0.14, and < 75 mm match to (-0.14); X_6 is postoperative change of LL: ⩾ 35° match to 0.07, and < 35° match to (-0.07); X_7 is postoperative change of PI-LL: ⩾ 35° match to 0.001, and < 35° match to (-0.001); X_8 is type of osteotomy: PSO match to 0.05, and SPO match to (-0.05); and X_9 is presence of postoperative pseudarthrosis: "yes", match to 0.17, and "no" match to (-0.17).

Table 7 Risk factors for mechanical complications of spine (all types: Vertebral fracture, proximal junctional failure, and distal segment degeneration/failure) after surgical correction of adult spinal deformity with osteotomy

Risk factor(s)	OR (95%CI: min; max)	*P* value	Predictive values			
			Sn	Sp	+PV	-PV
Postoperative SVA > 106 mm	11.3 (1.1; 118.1)	0.043	0.20	0.98	0.75	0.79
Type of osteotomy: SPO *vs* PSO	0.39 (0.1;1.1)	0.046	0.29	0.49	0.16	0.67
Fall after operation before mechanical complication	5.3 (1.6; 17.5)	0.006	0.33	0.91	0.57	0.80
Postoperative change of TK > 25° (absolute values)	4.8 (1.1; 20.8)	0.041	0.31	0.91	0.56	0.79
Postoperative change of PT > 8° (absolute values)	3.3 (0.9; 11.1)	0.045	0.69	0.60	0.38	0.84
Postoperative change of PI-LL > 34° (absolute values)	3.8 (0.9; 15.6)	0.065	0.31	0.89	0.50	0.79
Integral index by multiple regression modeling (1) ≥ 0.46	14 (2.7; 73.6)	< 0.001	0.85	0.72	0.50	0.93

SVA: Sagittal vertical axis; TK: Thoracic kyphosis; PT: Pelvic tilt; PI-LL: Pelvic incidence (PI)-lumbar lordosis (LL) mismatch; PSO: Pedicle subtraction osteotomy; SPO: Smith-Peterson osteotomy; OR: Odds ratio; 95%CI: min; max: 95% confidence limits, maximum and minimum values; Sn: Sensitivity; Sp: Specificity; +PV: Positive predictive value; -PV: Negative predictive value.

Factors that have significant association with MC of the spine include: Postoperative SVA > 107 mm, OR = 11.3 (95%CI: 1.1; 118.1), *P* = 0.043; type of osteotomy (SPO *vs* PSO), OR = 0.39 (95%CI: 0.1; 1.1), *P* = 0.046; fall after surgery, OR = 5.3 (95%CI: 1.6; 17.5), *P* = 0.006; postoperative change of TK > 25° in absolute values, OR = 4.8 (95%CI: 1.1; 20.8), *P* = 0.041; postoperative change of PT ⩾ 9° in absolute values, OR = 3.3 (95%CI: 0.9; 11.1), *P* = 0.049; postoperative change of PI-LL ⩾ 35° in absolute values, OR = 3.8 (95%CI: 0.9; 15.6), *P* = 0.059. The integral characteristic ⩾ 0.46 showed higher association, OR = 14.0 (95%CI: 27; 73.6), *P* < 0.001 (Table 7). Nevertheless, all these indices had limited predictive values, in particular, low Sn and +PV (Table 7). Prognostic capability of the integrative characteristic was somewhat better, but +PV was only 50% (Table 7).

Factors having significant association with VF were: smoking, OR = 5.7 (95%CI: 1.7; 19.1), *P* = 0.008; SPO *vs* PSO if osteotomy, OR = 0.25 (95%CI: 0.1; 0.8), *P* = 0.02; and fall after operation, OR = 4.3 (95%CI: 1.3; 14.5), *P* = 0.024 (Table 8). However, Sn and +PV of these variables was < 50% (Table 8). The integrative index had twice higher association, OR = 11.7 (96%CI: 2.2; 61.5), *P* < 0.001, as well as general prognostic capacity, but +PV was approximately the same (Table 8). Those factors having significant association with PJF included: Smoking, OR = 4.2 (95%CI: 1.0; 16.8), *P* = 0.05; SPO *vs* PSO of osteotomy, OR = 0.23 (95%CI: 0.05; 1.1), *P* = 0.041; a fall after the operation, OR = 4.2 (95%CI: 1.0; 16.8), *P* = 0.05; osteoporosis or osteopenia in cases treated with a PSO having > 5 fused levels, OR = 10.4 (95%CI: 0.8; 137.8), *P* = 0.039; reoperation *vs* primary operation, OR = 20.1 (95%CI: 2.5; 163.6), *P* < 0.001 (Table 8). However, all these characteristics had low +PV (< 30%) (Table 8). The integrative index did not show significant association with PJF, *P* = 0.167 (Table 8).

Factors having significant association with DSF included: preoperative LL ⩽ 20°, OR = 20.9 (95%CI: 2.3; 190.6), *P* = 0.002; crossing the thoracolumbar junction, OR = 18.6 (95%CI: 2.0; 164.9), *P* = 0.004; fixation to the sacrum or pelvis, OR = 0.08 (95%CI: 0.01; 0.73), *P* = 0.001 (Table 8). However, +PV of these characteristics was low (< 25%) (Table 8). The integrative index did not show significant association with DSF, *P* = 0.167 (Table 8).

Factors having significant association with MC of instrumentation were: Preoperative SVA ⩾ 100 mm, OR = 4.1 (95%CI: 1.5; 11.3), *P* = 0.007; postoperative change of SVA > 76 mm in absolute value, OR = 4.4 (95%CI: 1.1; 18.0), *P* = 0.041; postoperative SVA < 50 mm in cases with preoperative SVA > 110 mm, OR = 9.3 (95%CI: 1.4; 63.2), *P* = 0.025; crossing the thoracolumbar and/or lumbosacral junction(s), OR = 6.5 (95%CI:1.4; 30.2), *P* = 0.0.6; fixation to the sacrum and/or pelvis, OR = 4.0 (95%CI: 1.2; 12.1), *P* = 0.025; maximum rod contouring angle ⩾ 60°, OR = 4.4 (95%CI: 1.2; 16.1), *P* = 0.025; the use of rods individually precontoured by the manufacturer, OR = 0.35 (95%CI: 0.1;1.3), *P* = 0.05; use of more than 1 domino and/or parallel connectors, OR = 6.3 (95%CI: 0.5; 72.6), *P* = 0.06; preoperative LL ranging from 48° to 60°, OR = 0.15 (95%CI: 0.01; 1.3), *P* = 0.05; postoperative pseudarthrosis, OR = 9.2 (95%CI: 2.1; 39.3), *P* = 0.002, and the integrative index ⩾ 0.46, OR = 7.8 (95%CI: 2.0; 29.9), *P* = 0.002 (Table 9). In spite of the revealed statistically significant association the predictive capacity of all these characteristics was limited, in particular, +PV did not exceed 70% (Table 9).

The factors having significant association with SL included: Preoperative SVA > 100 mm, OR = 5.1 (95%CI: 1.6; 15.4), *P* = 0.005; postoperative change of SVA in absolute value > 76 mm, OR = 5.4 (95%CI: 1.3; 22.9), *P* = 0.026; postoperative SVA < 50 mm in cases with preoperative SVA > 110 mm, OR = 20.6 (95%CI: 2.6; 163.8), *P* = 0.004; fixation to sacrum and/or pelvis, OR = 2.5 (95%CI: 0.8; 8.3), *P* = 0.103; preoperative LL < 34°, OR = 3.4 (95%CI: 1.0; 10.9), *P* = 0.034; postoperative pseudoarthrosis, OR = 9.9 (95%CI: 2.4; 40.0), *P* = 0.001; rod fracture, OR = 15.6 (95%CI: 2.7; 89.8), *P* = 0.001; and the integrative index ⩾ 0.46, OR = 29.0 (95%CI: 3.3; 251.9), *P* < 0.001 (Table 10). The predictive capability of all these characteristics was limited, +PV ⩽ 71% (Table 10).

The factors having significant association with RF were: preoperative SVA > 100 mm, OR = 9.6 (95%CI: 1.7; 53.5), *P* = 0.008; postoperative change of SVA

Table 8 Risk factors for different mechanical complications of spine after surgical correction of adult spinal deformity with osteotomy

Mechanical complication of spine	Risk factors	OR (95%CI: min; max)	*P* value	Predictive values			
				Sn	Sp	+PV	-PV
Vertebral fracture	Current smoking	5.7 (1.7; 19.1)	0.008	0.37	0.91	0.50	0.85
	Type of osteotomy: SPO *vs* PSO	0.25 (0.1; 0.8)	0.020	0.21	0.48	0.09	0.71
	Fall after operation before mechanical complication	4.3 (1.3; 14.5)	0.024	0.32	0.89	0.43	0.84
	Integral index by multiple regression modeling (1) ⩾ 0.46	11.7 (2.2;61.5)	< 0.001	0.83	0.70	0.45	0.93
Proximal junctional failure	Current smoking	4.2 (1.0; 016.8)	0.055	0.36	0.88	0.29	0.91
	Osteoporosis/osteopenia	3.19 (0.9; 11.3)	0.075	0.55	0.72	0.21	0.92
	PSO and > 5 levels fused in osteoporosis/osteopenia	10.4 (0.8; 137.8)	0.039	1.00	0.84	0.29	1.00
	Fall after operation before mechanical complication	4.2 (1.0; 16.8)	0.055	0.36	0.88	0.29	0.91
	Reoperation *vs* primary operation	20.1 (2.5; 163.6)	< 0.001	0.92	0.65	0.28	0.98
	Type of osteotomy: SPO *vs* PSO	0.23 (0.05; 1.1)	0.048	0.18	0.51	0.05	0.82
	Integral index by multiple regression modeling (1) ⩾ 0.46	4.6 (0.4; 47.3)	0.167	0.75	0.60	0.14	0.97
Distal segmental degeneration/ failure	Preoperative LL ⩽ 20°	20.9 (2.3; 190.6)	0.002	0.83	0.81	0.23	0.99
	Thoracolumbar crossing junction	18.6 (2.0; 164.9)	0.004	0.83	0.78	0.21	0.99
	Fixation to sacrum or pelvic	0.08 (0.01; 0.73)	0.001	0.14	0.33	0.02	0.83
	Integral index by multiple regression modeling (1) ⩾ 0.46	2.9 (0.1; 89.1)	0.186	0.67	0.59	0.05	0.98

PSO: Pedicle subtraction osteotomy; SPO: Smith-Peterson osteotomy; OR: Odds ratio; 95%CI: min; max: 95% confidence limits with minimum and maximum values; Sn: Sensitivity; Sp: Specificity; +PV: Positive predictive value; -PV: Negative predictive value; LL: Lumbar lordosis.

Table 9 Risk factors for instrumentation failure (all types) after surgical correction of adult spinal deformity with osteotomy

Factors	OR (95%CI: min; max)	*P* value	Predictive values			
			Sn	Sp	+PV	-PV
Preoperative SVA ≥ 100 mm	4.1 (1.5; 11.3)	0.007	0.46	0.83	0.48	0.82
Postoperative change of SVA > 76 mm (absolute values)	4.4 (1.1; 18.0)	0.041	0.32	0.90	0.60	0.75
Postoperative SVA < 50 mm, if preoperative SVA⩾ 110 mm	9.3 (1.4; 63.2)	0.025	0.67	0.82	0.40	0.93
Preoperative LL 48°-60°	0.15 (0.01; 1.3)	0.043	0.05	0.76	0.07	0.67
Thoracolumbar and/or lumbosacral crossing junction(s)	6.5 (1.4; 30.2)	0.006	0.92	0.37	0.36	0.92
Fixation to sacrum and/or pelvic	4.0 (1.2; 12.8)	0.026	0.83	0.44	0.34	0.89
Maximum rod contouring angle > 60°	4.4 (1.2; 16.1)	0.025	0.62	0.73	0.40	0.87
Precontoured posterior rods *vs* in situ contouring	0.35 (0.1; 1.3)	0.050	0.38	0.36	0.16	0.65
Domino and/or parallel connectors number > 1	6.3 (0.5; 72.6)	0.063	0.08	0.99	0.67	0.76
Postoperative pseudarthrosis	9.2 (2.1; 39.3)	0.002	0.29	0.96	0.70	0.80
Integral index by multiple regression modeling (1) ⩾ 0.46	7.8 (2.0; 29.9)	0.002	0.75	0.72	0.55	0.87

SVA: Sagittal vertical axis; LL: Lumbar lordosis; Sn: Sensitivity; Sp: Specificity; +PV: Positive predictive value; -PV: Negative predictive value.

absolute value > 76 mm, OR = 11.3 (95%CI: 2.0; 63.3), *P* = 0.007; postoperative SVA < 50 mm in cases with preoperative SVA > 110 mm, OR = 33.0 (95%CI: 2.6; 424.1), *P* = 0.002; preoperative LL < 20°, OR = 4.9 (95%CI: 1.0; 24.3), *P* = 0.05; postoperative change of absolute values in LL ⩾ 30°, OR = 7.4 (95%CI: 1.3; 41.5), *P* = 0.022; postoperative pseudoarthrosis, OR = 8.6 (95%CI: 1.6; 46.2), *P* = 0.019; use of domino and/or parallel connectors, OR = 5.8 (95%CI: 1.1; 29.6), *P* = 0.052; sagittal rod contouring angle > 56°, OR = 9.8 (95%CI: 1.1; 85.2), *P* = 0.019; connecting to previously placed instrumentation, OR = 8.3 (95%CI: 1.7; 41.9), *P* = 0.014; iliac bolt connector loose and/or fracture, OR = 17.0 (95%CI: 1.9; 147.0), *P* = 0.026; the integrative index ⩾ 0.46, OR = 6.9 (95%CI: 0.7; 66.5), *P* = 0.027 (Table 10). The predictive value of these characteristics was limited, in particular, +PV ranged from 12% to 75% (Table 10).

The factors having significant association with IBCF included: Preoperative SVA > 100 mm, OR = 24.0 (95%CI: 1.6; 356), *P* = 0.02; and postoperative change in absolute value of SVA > 76 mm, OR = 7.4 (95%CI: 0.7; 81.4) > 8, *P* = 0.029. The integrative index did not show significant association with this type of MC (Table 11). The predictive capability was limited, +PV of these characteristics did not exceed 60% (Table 11).

Finally, factors having significant association with DI were: SPO *vs* PSO, if osteotomy applied, OR = 0.15 (95%CI: 0.02; 1.3), *P* = 0.050; osteotomy of the lumbar spine, OR = 7.4 (95%CI: 0.7; 81.4), *P* = 0.029; and fixation to sacrum and/or pelvis, OR = 4.80.2, *P* = 0.04, the integrative index did not show significant association with this type of MC, Table 11. The predictive capability was limited; +PV of these characteristics was ⩽ 40% (Table 11).

DISCUSSION

To evaluate the postoperative MC and associated risk factors after surgical correction of ASD with an

Table 10 Risk factors for screw loosening and rod fracture after surgical correction of adult spinal deformity with osteotomy

Instrumentation failure	Risk factors	OR (95%CI: min; max)	*P* value	Predictive values			
				Sn	Sp	+PV	-PV
Screw loosening	Preoperative SVA ⩾ 100 mm	5.1 (1.6; 15.4)	0.005	0.53	0.82	0.39	0.89
	Postoperative change of SVA > 76 mm (absolute values)	5.4 (1.3; 22.9)	0.026	0.38	0.90	0.50	0.84
	Postoperative SVA < 50 mm, if preoperative SVA ⩾ 110 mm	20.6 (2.6; 163.8)	0.004	0.67	0.91	0.57	0.94
	Preoperative LL < 34°	3.4 (1.0; 10.9)	0.034	0.69	0.61	0.31	0.88
	Fixation to sacrum and/or pelvic	2.5 (0.8; 8.3)	0.103	0.78	0.42	0.24	0.89
	Postoperative pseudarthrosis	9.9 (2.4; 40.0)	0.001	0.35	0.95	0.60	0.87
	Rod fracture	15.6 (2.7; 89.8)	0.001	0.29	0.97	0.71	0.86
	Integral index by multiple regression modeling (1) ⩾ 0.46	29.0 (3.3;251.9)	< 0.001	0.92	0.73	0.50	0.97
Rod fracture	Preoperative SVA ⩾ 100 mm	9.6 (1.7; 53.5)	0.008	0.71	0.79	0.22	0.97
	Postoperative change of SVA > 76 mm (absolute values)	11.3 (2.0; 63.3)	0.007	0.57	0.89	0.40	0.94
	Postoperative SVA < 50 mm, if preoperative SVA ⩾ 110 mm	33.0 (2.6; 424.1)	0.002	0.50	0.97	0.75	0.92
	Preoperative LL < 20°	4.9 (1.0; 24.3)	0.050	0.57	0.79	0.21	0.95
	Postoperative change of LL ⩾ 30°	7.4 (1.3; 41.5)	0.022	0.71	0.75	0.23	0.96
	Postoperative pseudarthrosis	8.6 (1.6; 46.2)	0.019	0.43	0.92	0.30	0.95
	Domino and/or parallel connectors	5.8 (1.1; 29.6)	0.052	0.43	0.89	0.23	0.95
	Sagittal rod contouring angle > 56°	9.8 (1.1; 85.2)	0.019	0.86	0.62	0.15	0.98
	Number of crossing junctions > 1	5.6 (0.7; 48.5)	0.087	0.86	0.48	0.12	0.98
	Connecting to previously implanted instrumentation	8.3 (1.7; 41.9)	0.014	0.57	0.86	0.25	0.96
	Iliac bolt connector loose and/or fracture	17 (1.9;147.0)	0.026	0.67	0.89	0.50	0.94
	Integral index by multiple regression modeling (1) ⩾ 0.46	6.9 (0.7; 66.5)	0.027	0.80	0.63	0.18	0.97

SVA: Sagittal vertical axis; LL: Lumbar lordosis; Sn: Sensitivity; Sp: Specificity; +PV: Positive predictive value; -PV: Negative predictive value.

Table 11 Risk factors for iliac bolt connector loosening/fracture and disassociation of instrumentation after surgical correction of adult spinal deformity with osteotomy

Instrumentation failure	Risk factors	OR (95%CI: min; max)	*P* value	Predictive values			
				Sn	Sp	+PV	-PV
Iliac bolt connector loosening/fracture	Preoperative SVA ⩾ 100 mm	24.0 (1.6; 356.0)	0.021	0.75	0.89	0.60	0.94
	Postoperative change of SVA > 76 mm (absolute values)	7.4 (0.7;81.4)	0.029	0.80	0.65	0.40	0.92
	Integral index by multiple regression modeling (1) ⩾ 0.46	4.69 (0.4; 47.3)	0.069	0.75	0.60	0.14	0.97
Disassociation of instrumentation	Type of osteotomy, SPO *vs* PSO	0.15 (0.02; 1.3)	0.050	0.13	0.51	0.02	0.86
	Lumbar osteotomy	7.4 (0.7; 81.4)	0.029	0.80	0.65	0.40	0.92
	Fixation to sacrum or pelvic	4.8 (0.6; 40.8)	0.039	0.88	0.41	0.12	0.97
	Integral index by multiple regression modeling (1) ⩾ 0.46	4.5 (0.4; 47.4)	0.069	0.75	0.60	0.14	0.97

SVA: Sagittal vertical axis; LL: Lumbar lordosis; SPO: Smith-Petersen osteotomy; PSO: Pedicle subtraction osteotomy; Sn: Sensitivity; Sp: Specificity; +PV: Positive predictive value; -PV: Negative predictive value.

osteotomy, a case-series of 94 consecutive operations performed in 88 patients were studied. The incidence of postoperative return to the operating room after the index surgery was 42.5%. The cumulative incidence of MC was 43.6%. The incidence of MC of the spine and MC of instrumentation were approximately similar, 25%. Of those, 16% of cases had multiple MC. The most typical MC of the spine were VF (20.2%), PJF (11.7%), and less common DSF (6.4%) (Figure 6 and Table 5). The most typical MC of instrumentation was SL (18.1%), other MC of instrumentation had incidence ranging from 2% to 7.4% (Figure 6 and Table 5).

Around 70% of all MC were diagnosed during the 1st postoperative year. The majority of MC with the shortest latent period were linked with failure of the spine (VF and PJF, where 70% of cases were revealed during 8 mo of follow-up) (Figure 7). Approximately the same latent period also showed higher rates of SL (specifically screw fracture) and DI (Figure 7). It is necessary to note that 2 cases of screw fracture observed in the current study were accompanied with fractures of the pedicle. The MC with a longer latent period (70% of cases were revealed at ⩾ 19 mo of follow-up) tended to be linked with instrumentation failure. This included RF, and IBCF (Figure 7). As expected, DSF had a longer latent period closer to that of IBCF (Figure 7).

The MC had significant association with postoperative return to the operating room (OR = 20.0). The strongest association showed MC of the spine, in particular: VF, PJF (OR ⩾ 19.0), and DSF (OR = 7.6). Among MC of instrumentation, significant association with secondary surgical treatment showed cases of SL (OR = 4.2) and DI (OR = 9.4). It may be explained by the fact that MC of the spine occurred early, preceding solid fusion, and provoked the corresponding severe clinical symptoms. Some of the MC of instrumentation,

in particular RF and IBCF occurred later. There were seen even after the development of solid intervertebral fusion. They were less likely to lead to spinal instability and clinical symptoms requiring surgical treatment.

The revealed characteristics that have significant association with increased risk of MC may be classified into subgroups. First, indices linked with severity of the preoperative sagittal imbalance including: SVA > 100°; and LL< 34°. Second, preoperative comorbidities such as: smoking, and osteoporosis/osteopenia (specifically, in cases after PSO with more than 5 levels fused). Third, postoperative events such as: a fall and pseudoarthrosis. The fourth subgroup reflects insufficient correction of the sagittal imbalance (postoperative SVA > 75 mm). The fifth group includes indices linked with over-correction of the sagittal imbalance and spinopelvic alignment or reciprocal changes including: Postoperative SVA < 50 mm, if preoperative SVA ⩾ 110 mm; postoperative changes in absolute values for SVA > 76 mm, TK > 25°, LL > 29°, PI-LL > 35°, and PT > 9°. Also, characteristics of the index operation and the surgical technique were associated with MC: Revision surgery, type of osteotomy (PSO), lumbar location of the osteotomy, crossing transitional spinal segments (thoracolumbar, lumbosacral, and > 1 junction crossed). The seventh group included characteristics of the instrumentation and the fusion construct including: Sagittal rod contouring > 60°, fixation to the sacrum or pelvis (specifically after PSO with > 5 level fused), use of dominos and/or parallel connectors, and connecting to the previously implanted instrumentation. Finally, the other device failures, in particular, RF associated with SL.

Off note, some factors had significant association with low risk of MC or had multiple effects. This was seen in particular with cases having preoperative LL ranging between 47° and 61° (showed lower risk of MC of instrumentation), fixation to the sacrum with or without fixation to pelvis increased risk of SL, but expected decreased risk of DSF, and use of rods individually precontoured by manufacturer decreased risk of MC of instrumentation.

Unlike previous investigators we regarded postoperative pseudarthrosis as a risk factor rather than a MC. This showed that pseudarthrosis was significantly association with MC of instrumentation, in particular SL and RF. This association may reflect progression of postoperative instability, which increases strain at the fused spinal segments preventing ossification of the callus and contributing to the risk of instrumentation failure.

The main results of the current study correspond with previous findings. The results revealed the incidence of pseudarthrosis, revision/reoperation, and severe PJF values very close to those previously reported[11,16,25]. The postoperative period of occurrence for PJF and RF also corresponded with the previously published time-frames[27,44]. It was demonstrated by Charosky *et al*[11] (2012) that the use of a PSO is associated with higher risk of MC. This corresponds with the results of the current study. However, an additional analysis has shown that a PSO (as expected) is more often applied in cases with severe preoperative sagittal imbalance (SVA ⩾ 100 mm). This high starting SVA is also a risk factor of MC, making the argument somewhat circular. Stratification demonstrated that in cases with a preoperative SVA < 100 mm, a PSO showed higher risk of MC than SPO (OR = 2.3; *P* = 0.1), while in the cases with the SVA ⩾ 100 mm this difference was absent (OR = 0.95; *P* = 0.96). It suggests that SPO has benefit only in cases with small or moderate sagittal imbalance. While this seems intuitive, this finding requires further confirmation due to the relatively small number of cases in the studied subgroups after the stratification. The same authors, previously cited, suggested that fixation to sacrum is associated with a higher risk of MC (OR = 3.7)[11]. The results of current study confirm this finding with important details: Fixation to sacrum with or without fixation to pelvis was associated with instrumentation failure (OR = 4.0, Table 9), in particular SL (OR = 2.5, Table 10). However, it simultaneously minimized risk of DSF as would be expected (OR = 0.08, Table 8). Inoue *et al*[16] (2015) showed that preoperative SVA > 95 mm is a risk factor of MC (HR = 2.6). Our results confirmed this finding with somewhat higher SVA threshold (SVA > 110 mm, OR = 4.5, Table 6). Combining of these findings by the Bayesian method suggested strong evidence (PO = 11.7) that severe preoperative anterior sagittal imbalance contributes to the risk of postoperative MC. Smoking was shown as a risk factor of MC (HR = 3.3)[16]. It was also confirmed by the present study, particularly for VF (OR = 5.7) and PJF (OR = 4.2), with a strong level of evidence by the Bayesian method (PO > 13.8). Smith *et al*[33] (2015) reported that postoperative SVA < 50 mm is a risk factor of PJF; however, adequate risk analysis and acceptable interpretation of this finding were not shown. The results of the current study have added details necessary for adequate interpretation of this finding. It was shown that the postoperative SVA < 50 mm can be associated with MC (SL), but specifically in patients with a preoperative SVA > 110 mm. This suggests significant correction, not SVA < 50 mm, is the more important factor to consider. Yagi *et al*[32] (2012) showed that progress of proximal junctional kyphosis is more significant in patients with osteoporosis. The results of present study confirmed the role of osteoporosis as a risk factor of PJF, specifically in cases after PSO and more than 5 levels fused. The obtained results regarding risk factors of RF are close to those previously published[27]. However, a few additional factors were revealed which are linked with severity of the preoperative sagittal imbalance and level of correction (Table 10). A relatively high incidence of SL appears contradictory to the experimental data, which showed that force around 1300N is necessary to cause pedicle screw failure. Supplemental hooks have not been shown to change this force[45]. Forces in the fusion construct are considerably less, but they act constantly during a long period of time which can cause permanent strain (micromotion).

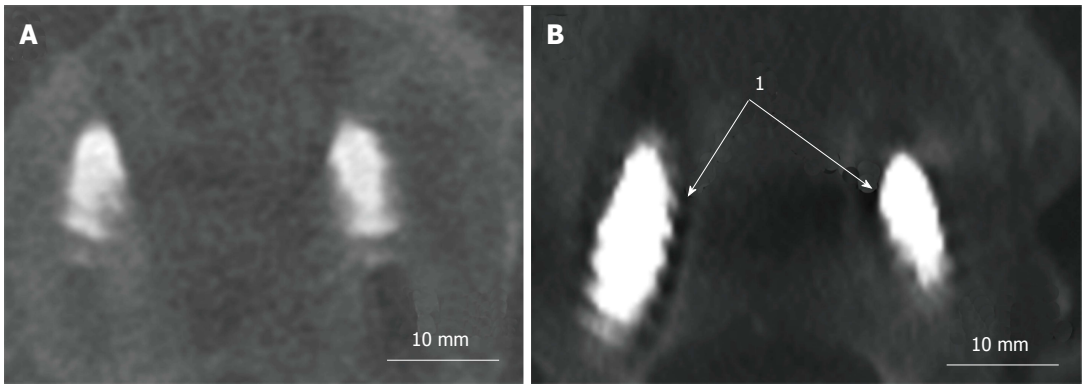


Figure 8 Failure of the bone-screw interface. This effect was observed in a 75-year-old male after surgical correction of adult spine deformity with T12-L2 instrumented fusion, L1/L2 Smith-Petersen osteotomy, and transforaminal interbody fusion. A: Postoperative pedicle screws placed at T12 with good contact between the screws and the bone (absence of noticeable radiolucency around the screws); B: Loosening of the screws with loss of boney fixation that was revealed at 6 mo follow-up. This effect is viewed as radiolucency around the screw (1). This may be due to bone resorption, starting the process of screw pullout at 6-mo follow-up.

This strain may stimulate bone remodeling, decreasing contact surface between screws and the bone[46,47]. Finally, it may result in screw pullout (Figure 8). This process may take anywhere from one to several months.

In the current study we did not reveal a significant association between MC and such demographic characteristics as age, gender and BMI unlike some previous studies[8,35-37]. It may be explained by more severe preoperative sagittal imbalance in the cases that were included in the present study. This suggests the impact of factors other than demographic data prevailed in the studied case series. Devices and techniques for preoperative planning of correction were recently introduced at our institution[48]. These utilize patient specific rods precontoured by the manufacturer according to a preoperative surgical plan. The present study has shown that the use of this approach decreases the risk of the instrumentation failure (Table 9).

Analysis of the risk factors as presented above allows assumption that permanent mechanical stress in the spine and in the implanted devices, as a result of spinal correction, is the main risk of MC. The mechanical strength of bone and ligaments is less than that of the instrumentation; therefore MC of the spine occurred earlier than MC of instrumentation. Other factors such as surgical technique, type of instrumentation, and preoperative health status of patient may significantly modify the effect of this constant stress. This statement corresponds well with the previous experimental data suggesting that stiff instrumentation, which provides stability, simultaneously increases strain in the construct through a physiologic range of motion[49]. There are therefore two main sources of the postoperative mechanical stress. First is proportional to the preoperative spinal deformity, sagittal imbalance, abnormality of the spinopelvic alignment, and the level of correction; second is caused by the patient's postoperative posture and motion. The first maybe increased by over-correction and the second may be worsened by insufficient correction. The combination of these 2 main effects causes somewhat contradictory results. An optimal balance between these two mechanical stresses is important to minimize the risk of the postoperative MC.

The results of the current and previous studies provide guidelines that may decrease the risk of postoperative MC. First, the absolute difference between postoperative and preoperative spinopelvic parameters should not exceed SVA > 75 mm, LL > 30°, TK > 25°, PI-LL > 30°, and PT > 9°. Second, postoperative anterior sagittal imbalance should not exceed 75 mm, and in patients with preoperative SVA > 110 mm, a postoperative SVA from 50 mm to 75 mm may be regarded as an acceptable. Third, in situ contouring of rods > 60° and repetitive contouring should be avoided. Fourth, the use of dominos and/or parallel connectors should be avoided or minimized. Fifth, the combination of pedicle screws with hooks may be appropriate in cases with preoperative SVA > 100 mm, having concomitant osteoporosis, and requiring significant correction with long posterior instrumented fusion (> 5 levels) and an osteotomy. Sixth, in cases with preoperative SVA < 100 mm, SPO is preferred to a PSO, if there is no specific indication for a PSO (such as ankylosing spondylitis) and adequate correction may be obtained. Finally, the use of preoperative planning with precontoured rods decreases the risk of instrumentation failure. The protective effect of this method may be enhanced by the application of optimal spinopelvic parameters, which provide criteria correction[50].

This study had several limitations, including the retrospective design with an inherent risk of selection bias and the incomplete/limited quality of the radiographic data, which may cause underestimation of significance for several of the studied risk factors. In particular, the role of sacral slope and pelvic incidence was not evaluated in the current study. The causes of the postoperative falls were not studied, and it is still unclear whether it was consequences of vestibular, vascular, mental or other diseases. The revealed risk factors, in spite of high statistical significance, had limited predictive capability, in particular, low positive predictive value. There may other risk factors that were not taken into consideration in the current study.

However, in spite of these limitations, the combination of obtained results with the previously published findings confirms the consistency of the revealed effects. Therefore, the presented results should be viewed as a grounded, preliminary basis for further research with higher levels of evidence.

Incidence of MC after surgical correction of ADS is relatively high, and often requires additional surgical treatment. To diminish the risk of MC, the correction of sagittal imbalance and spinopelvic alignment should be appropriate, over- and insufficient correction should be avoided. Treatment strategy, surgical technique, and instrumentation should be improved for cases with severe anterior sagittal imbalance, spine compromised by previous surgical interventions, and, specifically, with concomitant osteoporosis.

ARTICLE HIGHLIGHTS

Research background

It has been pointed out during last decades that mechanical complications (MC) after surgical correction of adult spine deformity (ASD) are most typical, and often require additional surgical treatment. However, these complications were not clearly defined. Their specific appearances, incidence, distribution by postoperative follow-ups, and risk factors were not studied well.

Research motivations

New knowledge concerning nature and causes of the MC would enable diminish their occurrence and improve postoperative clinical outcomes after surgical correction of ASD.

Research objectives

The main objectives of the study were identification of the most clinically relevant MC seen after surgical correction of ASD with corrective osteotomies, defining of their incidence, the most likelihood period of occurrence, association with additional surgeries; revealing of risk factors and assessment their predictive value. Achievement of these purposes would have enabled formulation of grounded recommendation to diminish risk of such complications and contribute to defining directions for further research in this field.

Research methods

The retrospective clinical study was performed. Medical records, operation protocols, and radiographic images were studied in patients who underwent surgical correction of adult spine deformity with osteotomy. Preoperative, perioperative, and postoperative data were collected for 2 and more years of follow-up. Postoperative mechanical failures of spine and implanted instrumentation were studied in detail including: their features, latent periods, incidence, required additional treatment, and different risk factors such as: Demographic, preoperative and postoperative spinopelvic alignment, level of correction, spinal instrumentation, features of surgical intervention, *etc*.

Research results

It was shown that around half of patients experienced MC during two postoperative years; majority of these cases required additional surgery. MC of spine occurred earlier and more often required revision than breakage of the instrumentation. The main risk factors included severe preoperative sagittal imbalance, inadequate correction of the spinopelvic alignment, preoperative comorbidities (osteoporosis, smoking), postoperative events (falls), and features of the spinal instrumentation. There was developed method that enables recognition of patients with high risk of postoperative MC.

Research conclusions

The performed study is first that performed a clear classification of the clinically relevant MC after surgical correction of ASD with osteotomy. In particular, there were specified those complications that are linked with failure of spine, breakage of the instrumentation; and disassociation between different elements of the spinal fusion construct. First time, impact of more than 50 potential risk factors of the MC and their combinations was assessed. There were revealed risk factors and their combinations that had statistically significant association with one or a few MC. The predictive value of each of these risk factors for each type of MC was evaluated. The obtained results allowed development of a new method to recognize patients with high risk of postoperative MC; and provide newel grounded recommendations to diminish risk of such complications. Implication for clinical practice: implementation of these methods can contribute to improvement of treatment outcomes after surgical correction of ASD with osteotomy, and diminish treatment expenses.

Research perspectives

The obtained results and recommendations require further confirmation by studies with higher level of evidence such as prospective cohort and randomized clinical trials. The predictive capability of the risk factors revealed in the current study showed underestimation of risk of MC after surgical correction of ASD. It suggests that other currently unknown risk factors likely also exist. Therefore, further researches are needed in this field to reveal these factors.

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SYSTEMATIC REVIEWS

Synthetic *vs* biologic mesh for the repair and prevention of parastomal hernia

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Abstract

AIM

To outline current evidence regarding prevention and treatment of parastomal hernia and to compare use of synthetic and biologic mesh.

METHODS

Relevant databases were searched for studies reporting hernia recurrence, wound and mesh infection, other complications, surgical techniques and mortality. Weighted pooled proportions (95%CI) were calculated using StatsDirect. Heterogeneity concerning outcome measures was determined using Cochran's Q test and was quantified using I^2. Random and fixed effects models were used. Meta-analysis was performed with Review Manager software with the statistical significance set at $P \leqslant 0.05$.

RESULTS

Forty-four studies were included: 5 reporting biologic mesh repairs; 21, synthetic mesh repairs; and 18, prophylactic mesh repairs. Most of the studies were retrospective cohorts of low to moderate quality. The hernia recurrence rate was higher after undergoing biologic compared to synthetic mesh repair (24.0% *vs* 15.1%, $P = 0.01$). No significant difference was found concerning wound and mesh infection (5.6% *vs* 2.8%; 0% *vs* 3.1%). Open and laparoscopic techniques were comparable regarding recurrences and infections. Prophylactic mesh placement reduced the occurrence of a parastomal hernia (OR = 0.20, $P < 0.0006$) without increasing wound infection [7.8% *vs* 8.2% (OR = 1.04, $P = 0.91$)] and without differences between the mesh types.

CONCLUSION

There is no superiority of biologic over synthetic mesh for parastomal hernia repair. Prophylactic mesh placement

during the initial surgery significantly reduces parastomal hernia occurrence regardless of the mesh type.

Key words: Parastomal hernia; Synthetic mesh repair; Biologic mesh repair; Prophylactic mesh repair

Core tip: This review and meta-analysis outlines all current evidence regarding prevention and treatment of parastomal hernia and compares the use of synthetic and biologic mesh. There is no superiority of biologic over synthetic mesh for parastomal hernia repair concerning parastomal hernia recurrence, wound infection and mesh infection. Prophylactic mesh placement during the initial surgery significantly reduces parastomal hernia occurrence regardless of the mesh type.

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INTRODUCTION

Parastomal hernia is a common complication of stoma formation during colorectal surgery, with incidences up to 50%. The risk of parastomal hernia is highest within the first few years after formation of the stoma but may develop as much as 20 years later[1]. Hernias are often asymptomatic and managed with conservative treatment. However, 11% to 70% of patients undergo surgery due to discomfort, pain, obstructive symptoms and cosmetic dissatisfaction[2]. These treatment percentages vary because surgeons are often reluctant to repair a parastomal hernia due to the high recurrence rate, complicated operation and co-morbidity of patients. Indeed, a parastomal hernia is regarded as a complex incisional hernia by hernia experts[3]. Hence, many patients suffer but never undergo surgery.

The recurrence rate of parastomal hernia is the lowest after mesh repair (0%-33%), whereas primary fascial closure (46%-100%) and relocation of the stoma (0%-76%) result in much higher rates. Although low recurrence rates are reported after synthetic mesh repair, concerns have been raised regarding the safety of synthetic meshes in (potentially) contaminated fields due to the risk of mesh infection and subsequent removal. Other mesh-related complications include chronic infection, bowel stenosis, erosion of the mesh through the bowel and skin and enteroatmospheric fistulisation. These complications led to the development of biologic mesh, which due to its bio-degradable nature, has the potential to ameliorate these problems in infected and contaminated fields.

The high prevalence of parastomal hernias and the difficulty of repair have led to a shift of focus from repair towards prevention using prophylactic mesh reinforcement at the time of stoma formation. However, prophylactic mesh placement coincides with risk of the same mesh-related morbidities of hernia repair.

There are no trials comparing biologic and synthetic mesh repair for parastomal hernias. Available studies show a large range in reported parastomal hernia recurrence rates and no difference in mesh type concerning hernia recurrence or infection resistance[4-7].

No clear answer can be given as to whether there is a difference between the outcomes of synthetic and biologic mesh repair. However, given the financial costs of biologic mesh, the evidence for superiority and more beneficial outcomes compared to synthetic mesh is mandatory to support its use.

There are various approaches regarding the anatomic position of the mesh during parastomal hernia repair. Meshes are implanted in an inlay, onlay, sublay or underlay (intraperitoneal) position. Laparoscopic repair involves the intraperitoneal technique, and open repair may involve any of the anatomical planes of the mesh. The inlay technique places the mesh within the fascial defect and is sutured to the fascial edges. With onlay repair, the mesh is placed subcutaneously and fixed onto the fascia of the anterior rectus sheath and the aponeurosis of the external oblique abdominal muscle. When using a retromuscular or sublay technique, the prosthesis is placed dorsally to the rectus muscle and anteriorly to the posterior rectus sheath after mobilization of the latter. When performing intraperitoneal repair, the choice can be made between the Sugarbaker and keyhole repair techniques. Regarding the Sugarbaker technique, the hernia defect is closed with intraabdominal placement of the prosthetic mesh securely sutured or tacked to the abdominal wall. Between the abdominal wall and the prosthesis, the bowel is lateralized passing from the hernia sac into the peritoneal cavity[8]. During keyhole mesh repair, a 2-3 cm hole is fashioned in the mesh for passage of the stoma, and the rest of the mesh covers the entirety of the hernia orifice, including sufficient overlap (5 cm beyond the edge of the hernia defect is recommended). Both the keyhole and Sugarbaker techniques can be performed open or laparoscopically[9,10].

The primary aim of the current study was to compare biologic and synthetic mesh use for the treatment and prevention of parastomal hernia by systematic review and meta-analysis of available data in the literature. The secondary aim was to evaluate the different anatomical positions and surgical techniques used for parastomal hernia repair. With the absence of rigorous data focused on hernia recurrence in the literature, this review contributes to the increased understanding of parastomal hernias.

MATERIALS AND METHODS

Search strategy

Articles for this review were identified by searching the electronic databases PubMed and Medline (January 1946 to present) and by manual cross-reference searches. The last search was performed on 19-4-2016. The search included the following terms: "Parastomal hernia", "Parastomal", "Paracolostomy", "Paraileostomy", "Stoma" and "Colostomy" to represent the population. These terms were combined with terms relevant to the outcomes, such as "Ventral hernia", "Defect", "Mesh", "Synthetic mesh", "Biologic mesh", "Closure", "Reconstruction", "Prosthesis", "Scaffold", "Prevention" and "Prophylactic". The full search strategy is provided in Appendix 1. No limitation to date or language was considered. Randomized and non-randomized studies were included. When multiple studies describing the same population were published, the most complete report was used. The systematic review was performed in accordance with PRISMA[11].

Critical appraisal

All selected papers were evaluated for methodological quality using the Cochrane risk-of-bias tool for randomized controlled trials and the Newcastle-Ottawa Scale (NOS) for all non-randomized and single group studies[12,13]. Assessment using the Cochrane risk-of-bias tool is based on sequence generation, allocation concealment, blinding of participants, personnel, outcomes assessors, incomplete outcomes data, selective outcomes reporting, and other sources of bias, such as baseline imbalance, early stopping bias, academic bias, and source of funding bias. The NOS is an instrument for assessing methodological quality and potential bias in non-randomized studies. A maximum of nine points were assigned to each study. Studies that scored four for selection, two for comparability, and three for assessment of outcomes were regarded as having a low risk of bias. Studies with two or three stars for selection, one for comparability, and two for outcome were considered as having a medium risk of bias. Any study with a score of one for selection or outcome, or zero for any of the three domains, was deemed as having a high risk of bias. A modification in the NOS was made for single group studies, which consisted of excluding the points for comparability with a maximum of six points: three for selection and three for outcome. After screening titles and abstracts, two reviewers (Knaapen L and Slater NJ) independently reviewed full-text articles for eligibility using the critical appraisal approach. Any disagreement was resolved by consensus with a third reviewer (van Goor).

Outcome measures

Studies were identified according to the following inclusion criteria: Participants (human adults, minimum of 18 years of age), intervention (parastomal hernia repair with a synthetic or biologic mesh and prophylactic placement of mesh), and sufficient data available (10 or more patients).

The following criteria were used for exclusion: Stoma relocation, primary suture repair, and unspecified surgical technique. Studies published only as abstracts were excluded because quality assessment could not be performed.

The primary outcome measure was the recurrence rates of parastomal hernia as defined by the respective authors. Secondary outcomes were wound infection, mesh infection, mortality, other complications (medical and surgical), anatomic position of the prosthesis and surgical approach (open or laparoscopic).

Data extraction and statistical analysis

All full-text articles that met the inclusion criteria were thoroughly reviewed, and the data for primary and secondary outcomes were extracted and recorded in a data form. Year of publication, study period, level of evidence, mean age, gender, number of patients included and evaluated, type of stoma, surgical technique (open or laparoscopic, anatomical mesh position, keyhole or Sugarbaker), type of mesh (biologic or synthetic) and duration of follow-up were also noted. Weighted pooled proportions with a 95%CI were determined for recurrence, wound infection, mesh infection, other complications and mortality using StatsDirect statistical software[14]. The heterogeneity concerning the outcome measures was determined with Cochran's Q test and quantified using I^2. A random-effects model was used unless heterogeneity was 0%, in which case, a fixed-effects model was used. Meta-analysis was performed using Review Manager[15] with the statistical significance set at $P < 0.05$.

RESULTS

A flowchart overview of the search including reasons for exclusion of studies is shown in Figure 1. A total of 44 studies were included. Five studies provided information on 84 biologic mesh repairs; 21 studies, on 669 synthetic mesh repairs; and 18 studies, on 500 prophylactic mesh placements.

The following were included in the current study: Seven randomized controlled studies (level 1 evidence; all prophylactic mesh repair), 5 non-randomized comparative studies (level 2 evidence) and 32 single-group studies (level 3 evidence). Concerning the risk of bias assessment of seven randomized controlled trials (Figure 2): Sequence generation was unclear in 4 (57%) and low in 3 (43%) studies; allocation concealment was unclear in 1 (14%) and low in 6 (86%) studies; performance bias was high in all 7 (100%) studies; detection bias was low in 3 (43%) and high in 4 (57%) studies; attrition bias was low in all 7 (100%) studies; reporting bias was low in 6 (86%) and high in 1 (14%) study; and other bias was unclear in 2 (29%), low in 3 (43%) and high in 2 (29%) studies.

The Newcastle-Ottawa Scale for quality assessment

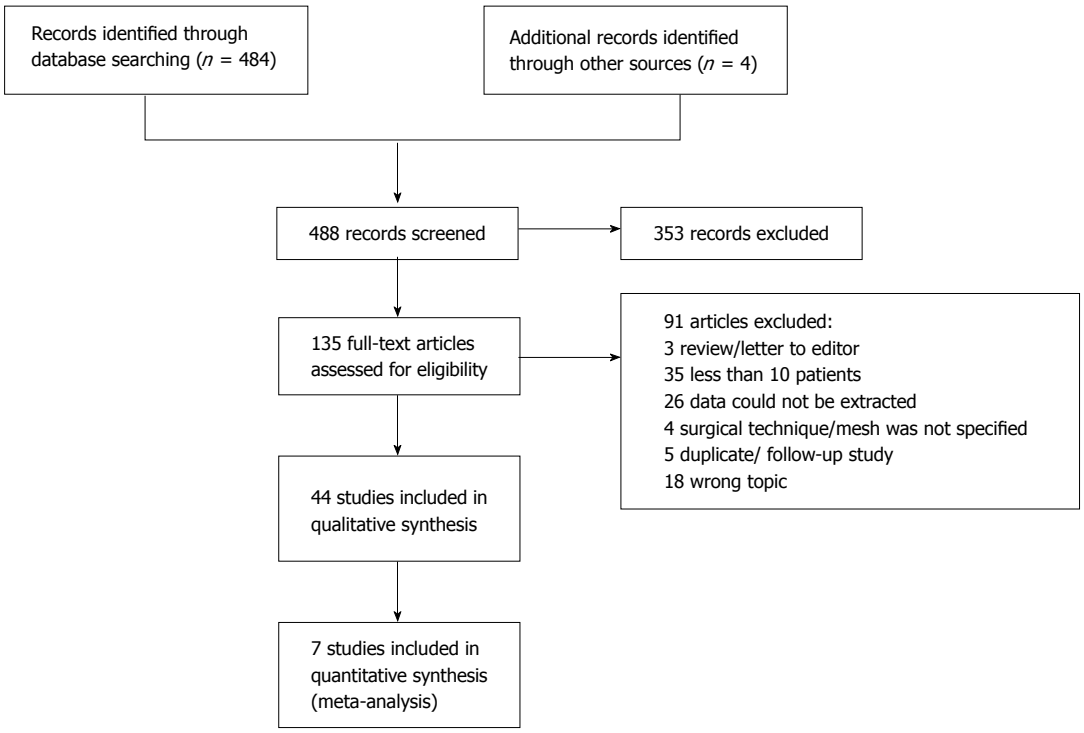

Figure 1 Search flow-chart following PRISMA.

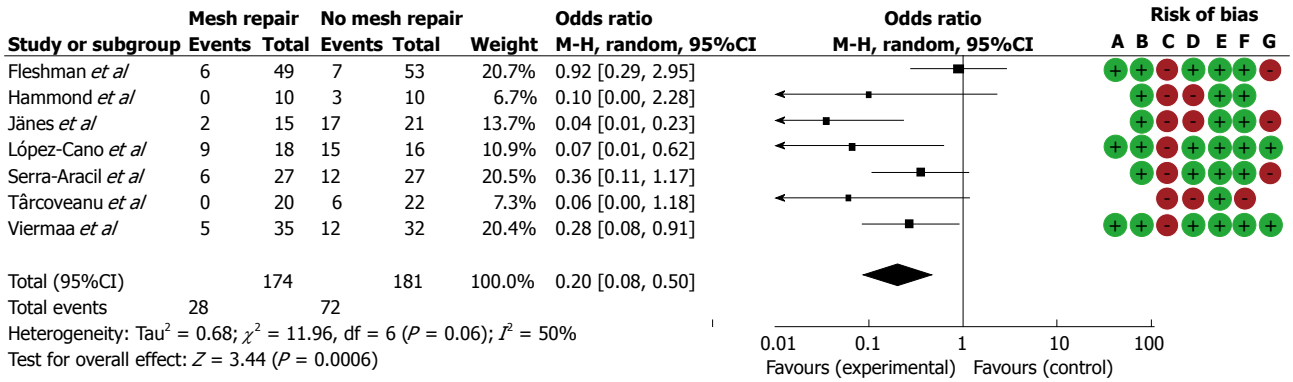

Figure 2 Incidence of parastomal hernia after prophylactic mesh placement *vs* no mesh placement. A: Random sequence generation (selection bias); B: Allocation concealment (selection bias); C: Blinding of participants and personnel (performance bias); D: Blinding of outcome assessment (detection bias); E: Incomplete outcome data (attrition bias); F: Selective reporting (reporting bias); G: Other bias.

showed that all 37 non-randomized studies had a low risk of bias for study selection. The five non-randomized two-group studies showed a low risk of bias regarding comparability in 1 study (20%), medium risk in 2 studies (40%), and high risk in 2 studies (40%). The risk of bias for outcome assessment was low in 20 (54%) studies, medium in 15 (41%) studies, and high in two (5%) studies (Figure 3).

Use of funding was not reported in 32 studies (73%). Five studies (11%) reported no funding[2,5,8,16,17]. Industry sponsored 4 biologic mesh studies (9%)[4,18-20]. The manufacturer supplied the mesh material in one biologic and one synthetic mesh study (5%)[21,22]. The state funded one study without financial disclosures reported[23]. Fifty-three percent of patients were female, and the mean age was 64.6 years. The indication for stoma placement was reported in 32 studies: benign disease in 9%, malignant disease in 68%, inflammatory bowel disease or diverticulitis in 19% and other causes in 4%. Patient demographics, study characteristics and critical appraisals are described in Table 1.

Biologic mesh repair of parastomal hernias

Biological grafts used in the included studies were Surgisis, AlloDerm, Permacol and Peri-Guard (Table 2). Five retrospective studies reported parastomal hernias that were repaired with a biologic mesh and included a combined enrolment of 84 patients. Patient follow-up ranged from 9-50 mo. One case of mortality was reported due to renal failure unrelated to the mesh[4]. Study characteristics and outcomes, including weighted-pooled rates of recurrence and wound-re-

Table 1 Patient demographics, study characteristics and critical appraisal of included studies

Ref.	Year	Inclusion period	Level of evidence	Mean age, years	Male (%)	Newcastle-Ottawa Scale			Cochrane risk of bias						
Târcoveanu *et al*[44]	2014	2010-2011	1	NS	NS				?	?	-	-	+	-	?
Ventham *et al*[63]	2012	2003-2010	2	I: 69, C: 68	I: 42%, C: 35%	****	**	***							
Hansson *et al*[8]	2013	2005-2010	3	63	35%	***		***							
López-Cano *et al*[40]	2012	2007-2010	1	I: 72, C: 66	I: 58%, C: 42%				+	+	-	+	+	+	+
Hauters *et al*[16]	2012	2008-2010	3	69 (median)	40%	***		***							
Fei *et al*[34]	2012	2008-2010	3	63	45%	***		***							
Mizrahi *et al*[2]	2012	2005-2010	3	64	34%	***		***							
Wara *et al*[5]	2011	1997-2008	3	62 (median)	50%	***		***							
Janson *et al*[64]	2010	2003-2007	3	65	40%	***		**							
Jänes *et al*[42]	2010	2003-2006	2	63	66%	****		**							
Pastor *et al*[26]	2009	1999-2006	2	I: 60, C: 54	I: 42%, C: 54%	****	*	***							
Lüning *et al*[65]	2009	1997-2006	3	65	27%	***		**							
Serra-Aracil *et al*[6]	2009	2004-2006	1	I: 68, C: 67	I: 70%, C: 59%				?	+	-	+	+	+	-
Hansson *et al*[31]	2009	2002-2006	3	63	49%	***		***							
Vijayasekar *et al*[45]	2008	2002-2007	3	61	52%	***		***							
Jänes *et al*[43]	2009	2001-2003	1	I: 70, C: 71	I: 56%, C: 59%				?	+	-	-	+	+	-
Berger *et al*[35]	2009	2004-2008	3	69 (median)	NS	***		***							
Muysoms *et al*[27]	2008	2001-2007	2	70	54%	****	*	***							
Guzmán-Valdivia *et al*[32]	2008	NS	3	67	64%	***		**							
Berger[39]	2008	2006-2007	3	72 (median)	64%	***		**							
Craft *et al*[66]	2008	2004-2006	3	66	NS	***		***							
Berger *et al*[7]	2007	1999-2006	3	70 (median)	39%	***		***							
Mancini *et al*[29]	2007	2001-2005	3	60	44%	***		**							
Marimuthu *et al*[46]	2006	2002-2005	3	67	44%	***		**							
Gögenur *et al*[22]	2006	2003-2005	3	71 (median)	60%	***		**							
van Sprundel *et al*[37]	2005	2000-2003	3	57	31%	***		***							
de Ruiter *et al*[33]	2005	1988-2002	3	NS	NS	***		***							
Longman *et al*[67]	2005	2000-2004	3	NS	NS	***		**							
LeBlanc *et al*[28]	2005	NS	3	42-89	NS	***		***							
Stelzner *et al*[36]	2004	1994-2002	3	70 (median)	60%	***		**							
Steele *et al*[30]	2003	1988-2002	3	64	50%	***		***							
Hofstetter *et al*[38]	1998	NS	3	NS	NS	***		***							
Viermaa *et al*[23]	2015	2010-2013	1	I: 67 C: 65	I: 51% C: 54%				+	+	-	+	+	+	+
Asif *et al*[17]	2012	2004-2011	3	62	60%	***		**							
Figel *et al*[62]	2012	2005-2008	3	63	67%	***		**							
Smart *et al*[4]	2011	2007-2009	3	72 (median)	44%	***		*							
Taner *et al*[25]	2009	2006-2007	3	NS	39%	***		**							
Hammond *et al*[68]	2008	NS	1	I: 43, C: 50	I: 30%, C: 40%				?	+	-	-	+	+	?
Hammond *et al*[21]	2008	NS	3	NS	NS			*							
Aycock *et al*[18]	2007	2004-2006	3	56	36%	***		**							
Araujo et al[24]	2005		3	57	27%	***		***							
Ellis *et al*[19]	2010	2004-2007	3	64	65%	***		***							
Fleshman *et al*[20]	2014	2010-2012	1	I: 60, C: 59	I: 55%, C: 50%				+	+	-	+	+	+	-
Williams *et al*[41]	2015	2011-?	2	I: 49, C: 59	I: 27%, C: 45%	***		**							

Level of evidence: 1: (Systematic reviews, meta-analyses) randomized controlled trials; 2: Two groups, non-randomized studies (*e.g.*, cohort, case-control); 3: One group, non-randomized; 4: Descriptive studies that include analysis of outcomes; and 5: Case reports and expert opinion that include narrative reviews and consensus statements. NS: Not significant.

lated complications, are shown in Table 3. Five studies reported 23 hernia recurrences with a weighted-pooled proportion of 24% (95%CI: 8.6-44.1) (Figure 4). Only three of these studies reported treatment after recurrence. Araujo *et al*[24] relocated the stoma and, Ellis *et al*[19] reported a reoperation using a bioprosthetic not further specified. Taner *et al*[25] reported two asymptomatic recurrences that were both treated conservatively. There were 4 wound infections that were reported with a weighted-pooled proportion of 5.6% (95%CI: 1.4-12.1)[4,18,25]. One was conservatively treated, one was treated with systemic antibiotics, and two were treated with local wound care[4,18,25]. No mesh infections were reported [0% (95%CI: 0-5.4)]. Other complications [13.4% (95%CI: 1.9-32.7)] were minor complications, including six seroma formations (four treated by drainage and two conservatively treated).

Synthetic mesh repair of parastomal hernias

Characteristics of the synthetic mesh used in the included studies are given in Table 2. One of the 21 studies was a prospective trial that recruited 12 patients with synthetic mesh repair and 13 control patients without mesh repair. The other 20 studies had a combined enrolment of 669 patients with synthetic mesh repairs[26]. Patient follow-up ranged from 7 to 51 mo.

Table 2 Characteristics of synthetic and biologic prostheses used for parastomal hernia repair

Name	Material	Coating	Absorbable	Pore size	Weight
StomaMesh Surgipro Prolene Central ring enforced polypropylene	Polypropylene	None	No	Small to medium 0.8 mm or large 1.0-3.6 mm	Heavy weight or light weight
DUALMESH	Composite multifilament expanded polytetrafluoroethylene	None	No	Very small 3/22 μm	Heavy weight
Proceed	Polypropylene Encapsulated in polydioxanone	Oxidized regenerated cellulose	Partially 180 d and 28 d	Large	Light weight
Parietex	Composite multifilament Polyester/collagen	Type I collagen, polyethylene glycol, and glycerol layer	Partially 20 d	Large > 3 mm	Medium weight
ULTRAPRO	Composite monofilament Polypropylene	Poliglecaprone-25 (monocryl)	Partially 140 d	Large > 3 mm	Light weight
VICRYL	Multifilament polyglactin	None	Yes, 60-90 d	Small 0.4 mm	Medium weight
Vypro	Polypropylene	PG910	Partially 42 d	Large > 3 mm	Light weight
Composix Parastomal hernia patch	Polypropylene/expanded polytetrafluoroethylene	None	No	Medium 0.8 mm	Light weight
DynaMesh	Polypropylene	PVDF	Partially	Large 1-2 mm	Medium weight
Surgisis	Porcine small intestine submucosa	None			
AlloDerm	Human acellular dermis	None			
Permacol	Cross-linked acellular porcine collagen	Yes, hexamethylene diisocyanate			
Peri-Guard	Bovine pericardium	Yes; glutaraldehyde			
STRATTICE	Non-crosslinked porcine-derived acellular dermal matrix	None			

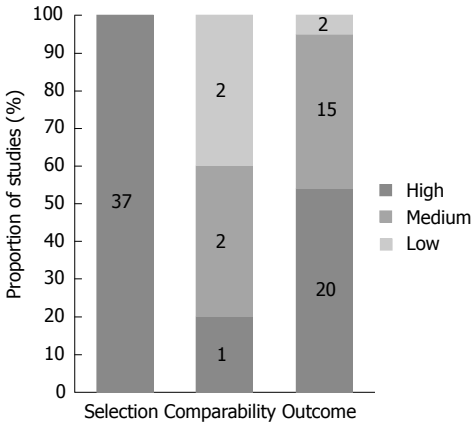

Figure 3 Quality assessment using the Newcastle-Ottawa Scale for risk of bias included in the systematic review. The absolute numbers of the studies are shown in boxes.

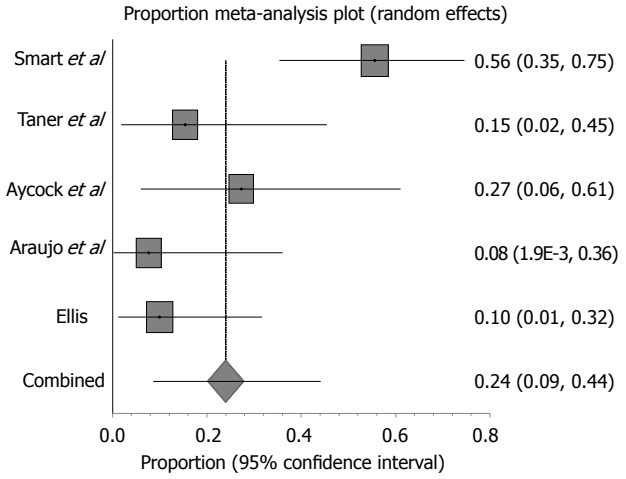

Figure 4 Proportion of hernia recurrences after biologic mesh repair of parastomal hernia. The square shape represents the weight of the study, and the horizontal line through the square represents the confidence interval of the effect estimate (random effects model; Cochran's *Q* test = 15.8; I^2 = 74.7%; *P* = 0.0033).

One study did not specify mean or median follow-up. The overall mortality was 1.9% (11 patients, weighted-pooled proportion, 95%CI: 0.9-3.2). None of the deaths were related to the mesh. Four post-operative deaths were due to progressive metastatic disease, two deaths were due to aspiration and subsequent cardiopulmonary arrest, and two deaths were due to secondary cardiopulmonary complications[8,27-29]. Wara *et al*[5] reported one death due to a neglected bowel injury that resulted in multiorgan failure and another death due to uncontrollable bleeding that resulted from portal hypertension that was unknown prior to surgery. One post-operative death was reported by Mizrahi *et al*[2] following sepsis that was not further specified and caused by an infected retroperitoneal haematoma, which necessitated a second operation.

Study characteristics and outcomes, including weighted pooled rates of recurrence and wound-related complications, are shown in Table 3. Nineteen studies

Table 3 Study characteristics and outcomes of synthetic mesh and biologic mesh repair of parastomal hernia *n* (%)

Ref.	No. patients (completed follow-up)		Type of stoma	Material; technique	Recurrence of parastomal hernia[1]		Wound infection		Mesh infection	Other[3]		Mortality	Follow-up (mo)
	Mesh	No mesh			Mesh	No mesh	Mesh	No mesh	Mesh	Mesh	No mesh		
Hansson *et al*[8]	61	-	C: 55 I: 4 U: 2	L: 55; IPOM: SB; ePTFE	4 (7)	-	1 (2)	-	1 (2)	21 (34)	-	1[2] (2)	26
Fei *et al*[34]	11	-	C: 6 I: 5	O: 11 Sublay: K; PP	1 (9)	-	0	-	NS	3 (27)	-	0	24
Mizrahi *et al*[2]	29 (28)	-	C: 18 I: 10 U: 1	L: 29 IPOM: K; ePTFE	13 (46)	-	NS	-	1 (4)	3 (11)	-	1[2] (4)	28
Wara *et al*[5]	72	-	C: 48 I: 24	L: 72 IPOM: K; PP+ePTFE	2 (3)	-	1 (1)	-	3 (4)	20 (28)	-	2[2] (3)	36
Pastor *et al*[26]	12	13	C: 10 I: 15	L: 12 O: 13 IPOM: K 3 SB: 7, lateral slit: 1 e-PTFE	4 (33)	7 (54)	2 (17)	2 (15)	0	1 (8)	0	0	14
Lüning *et al*[65]	15	-	C: 12 I: 3	O: 16 Onlay PP 7; PE 6; VICRYL 1; CRE-PPM 2	3 (20)	-	0	-	1 (7)	1 (7)	-	NS	33
Hansson *et al*[31]	55	-	C: 47 I: 5 U: 3	L 55 IPOM; K ePTFE	20 (36)	-	0	-	2 (4)	29 (53)	-	0	36 (median)
Berger *et al*[35]	47	-	NS	L: 46 O: 1 Sandwich PVDF-PP	1 (2)	-	1 (2)	-	NS	3 (6)	-	0	20 (median)
Muysoms *et al*[27]	24	-	C:20 I: 4	L: 24 IPOM K:11 non-slit SB 13 Parietex 11; DUALMESH 10; Composix 3	10 (42)	-	NS	-	NS	2 (8)	-	5[2] (21)	K: 31 SB: 14
Guzmán-Valdivia *et al*[32]	25	-	C:25	O: 25; Sublay PP	2 (8)	-	2 (8)	-	0	2 (8)	-	0	12
Craft *et al*[66]	21	-	C: 5 I: 7 U: 9	L: 21; IPOM K: 5 SB: 16 DUALMESH	1 (5)	-	1 (5)	-	2 (10)	8 (38)	-	0	14
Berger *et al*[7]	66	-	C:58 I:7 U:1	L: 66; IPOM SB: 41 Sandwich: 25 DUALMESH (until 4-2004) and Polyvinylidene	8 (12)	-	1 (2)	-	2 (3)	5 (8)	-	0	24 (median)
Mancini *et al*[29]	25	-	C: 15 I: 5 U: 6	L: 25; IPOM SB DUALMESH	1 (4)	-	1 (4)	-	1 (4)	3 (12)	-	1[2] (4)	19 (median)
van Sprundel *et al*[37]	16	-	C: 8 I: 5 U: 4	O: 16; IPOM K DUALMESH	1 (6)	-	0	-	0	5 (31)	-	0	29 (median)
de Ruiter *et al*[33]	46	-	C: 46	O: 46 Onlay CRE-PPM	7 (15)	-	0	-	3 (7)	2 (4)	-	0	51
Longman *et al*[67]	10	-	C: 7 I: 3	O: 10 Sublay K PP	0	-	0	-	0	1 (10)	-	0	30 (median)
LeBlanc *et al*[28]	12	-	C: 8 I: 2 U: 2	L: 12 IPOM SB 7, K 5 e-PTFE	1 (8)	-	0	-	0	2 (17)	-	1[2] (8)	20
Stelzner *et al*[36]	20 (19)	-	C: 20	O: 20 IPOM SB e-PTFE	3 (16)	-	1 (5)	-	0	3 (16)	-	0	42
Steele *et al*[30]	58	-	C: 31 I: 27	O: 58 Onlay "Stove pipe hat" PP	15 (26)	-	2 (3)	-	0	9 (16)	-	0	51
Hofstetter *et al*[38]	13	-	C: 13	O: 13 IPOM K e-PTFE	0	-	0	-	0	0	-	0	NS

Asif *et al*[17]	33		C: 12 I: 21	L: 33 SB:14 K:19 DUALMESH	11 (33)[4]	-	4 (12)		0	9 (27)		0	SB: 7 K: 36
Weighted pooled % (95%CI)					15.1% (9.7-21.6)		2.8% (1.6-4.4)		3,1% (1.8-4.6) FE	17,8% (12.0-24.4)		1.9 (0.9-3.2)	
Smart *et al*[4]	27	-	C: 20 I:7	O: 20 Onlay: K; Permacol	15 (55)	-	1 (4)	-	0	0	-	1[2] (4)	17
Taner *et al*[25]	13	-	NS	O: 13 Overlay + Underlay (sandwich) AlloDerm	2 (15)	-	1 (8)	-	0	4 (31%)	-	0	10
Aycock *et al*[18]	11	-	C:2 I:9	O: 11 Inlay 8; Onlay 3; AlloDerm	3 (27)	-	2 (18)	-	NS	1 (9)	-	0	9
Araujo *et al*[24]	13	-	C: 13	O: 13 Onlay; Peri-Guard	1 (8)	-	0	-	NS	NS	-	0	50
Ellis[19]	20	-	C: 17 I: 3	O: 20 IPOM; SB; Surgisis	2 (10)	-	0	-	0	4 (20)	-	0	18
Weighted pooled % (95%CI)					24% (8.6-44.1)		5.6% (1.4-12.1)		0% (0-5.4) FE	13.4% (1.9-32.7)		2.6% (0.3-6.9) FE	

Synthetic mesh repair: [1]With regard to lost after follow-up; [2]Unrelated to mesh; [3]Seroma 41 (48, 74, 121, 149, 171, 178, 201, 257); Cardiopulmonary 11 (48, 121, 171, 203, 487); Urinary tract infection 1 (243); Cutaneous/ fascial dehiscence 1 (252); Stoma complication 8 (121, 243, 245, 285); Ileus 13 (48, 87, 171, 212, 272); Post-operative bleeding 5 (48, 121, 171); Haematoma 6 (74, 171); Bowel stenosis 19 (121, 161, 178, 203, 207, 243, 272, 285, 487); Fistula formation 2 (285); Renal failure 4 (179, 203); Peritonitis 3 (121, 171); Other 18 (87, 171, 203, 207, 212, 243, 257, 272, 487); [4]All keyhole. Biologic mesh repair: [1]With regard to lost after follow-up; [2]Unrelated to mesh; [3]Complications other: Seroma 6 (165, 429), Incisional separation 2 (165), Epidural infection 1 (242). FE: Fixed-effect model. L: Laparoscopic; O: Open; C: Colostomy; I: Ileostomy; SB: Sugarbaker; K: Keyhole PP: Polypropylene mesh; IPOM: Intraperitoneal mesh; PCM: Parietex composite mesh; ePTFE: Expanded polytetrafluoroethylene; CRE-PPM: Central ring enforced polypropylene mesh; PP + ePTFE: Polypropylene-based mesh covered with ePTFE.

reported 108 hernia recurrences after mesh repair with a weighted-pooled proportion of 15.1% (95%CI: 9.7-21.6) (Figure 5). From the 19 studies that described hernia recurrence, 10 studies reported treatment. Three studies described 34 reoperations because of symptomatic hernia not further specified[30-32]. Two studies reported 2 patients who required reoperation that involved relocation of their stoma and mesh repairs[27,28]. Van Sprundel *et al*[33] noted one hernia recurrence due to a wide circle cut in the mesh, and in a second operation, the hernia content was removed, and the circle was narrowed with sutures. Ruiter and co-workers reported 5 patients who had the prosthesis definitively removed (not specified), 1 patient who had a smaller-sized prosthesis implanted and 1 patient who had only the hernia sac closed after midline laparotomy. Muysoms *et al*[27] noted one patient with a recurrence in whom a second laparoscopy was performed because of obstructive symptoms and was treated with a modified Sugarbaker technique. Another patient needed a laparotomy for a colonic abscess due to Crohn's disease. After colonic resection and mesh removal, a translocation of the colostomy was performed. Two reoperations for parastomal hernia recurrences were described by Fei *et al*[34] and Berger *et al*[35] due to the breakdown of the sutures used for closing and keeping the mesh in place. Berger *et al*[35] reported three other patients who were treated with the sandwich technique and one with the Sugarbaker technique. All other described hernia recurrences were asymptomatic and treated conservatively.

Surgical wound infection was mentioned in eleven studies reporting 17 patients with a weighted-pooled proportion of 2.8% (95%CI: 1.6-4.4). Four studies reported treatment of wound infection[5,26,29,32]. Two patients were treated by surgical drainage, and five were treated with systemic antibiotics. Pastor *et al*[26] reported 1 patient with a parastomal abscess and subsequent fistula development repaired by laparotomy, transection of the fistula tract, and re-siting of the ileostomy[26]. Sixteen mesh infections were observed with a weighted-pooled proportion of 3.1% (95%CI: 1.8-4.6), resulting in mesh removal from 14 patients. Other complications [17.8% (95%CI: 12.0-24.4%)] were seroma (31.1%), cardiopulmonary event (8.3%), urinary tract infection (0.8%), cutaneous/fascial dehiscence (0.8%), stoma complications (6.1%), ileus (9.9%), peritonitis (2.3%), post-operative bleeding (3.8%), haematoma (4.5%), bowel stenosis (14.4%), fistula formation (1.5%), renal failure (3%) and other (13.6%). Five of the 41 seromas were treated by surgical drainage, 12 were conservatively treated, and 24 did not have any reported treatment[8,32,34,35].

Comparison of biologic mesh repair and synthetic mesh repair: When comparing the prevalence of

Table 4 Summary of pooled proportions of outcome measures of biologic mesh repair *vs* synthetic mesh repair

Hernia repair	No of studies	No of mesh repairs	Recurrence	Complications		
				Wound infection	Mesh infection	Other
Biologic mesh	5	84	24% (8.6-44.1)	5.6% (1.4-12.1)	0% (0-5.4) FE	13.4% (1.9-32.7)
Synthetic mesh	21	669	15.1% (9.7-21.6)	2.8% (1.6-4.4)	3.1% (1.8-4.6) FE	17.8% (12.0-24.4)
P value			0.01	0.32	0.39	0.15

Two-tailed Fisher's exact test was used because of too small frequencies. FE: Fixed-effect model.

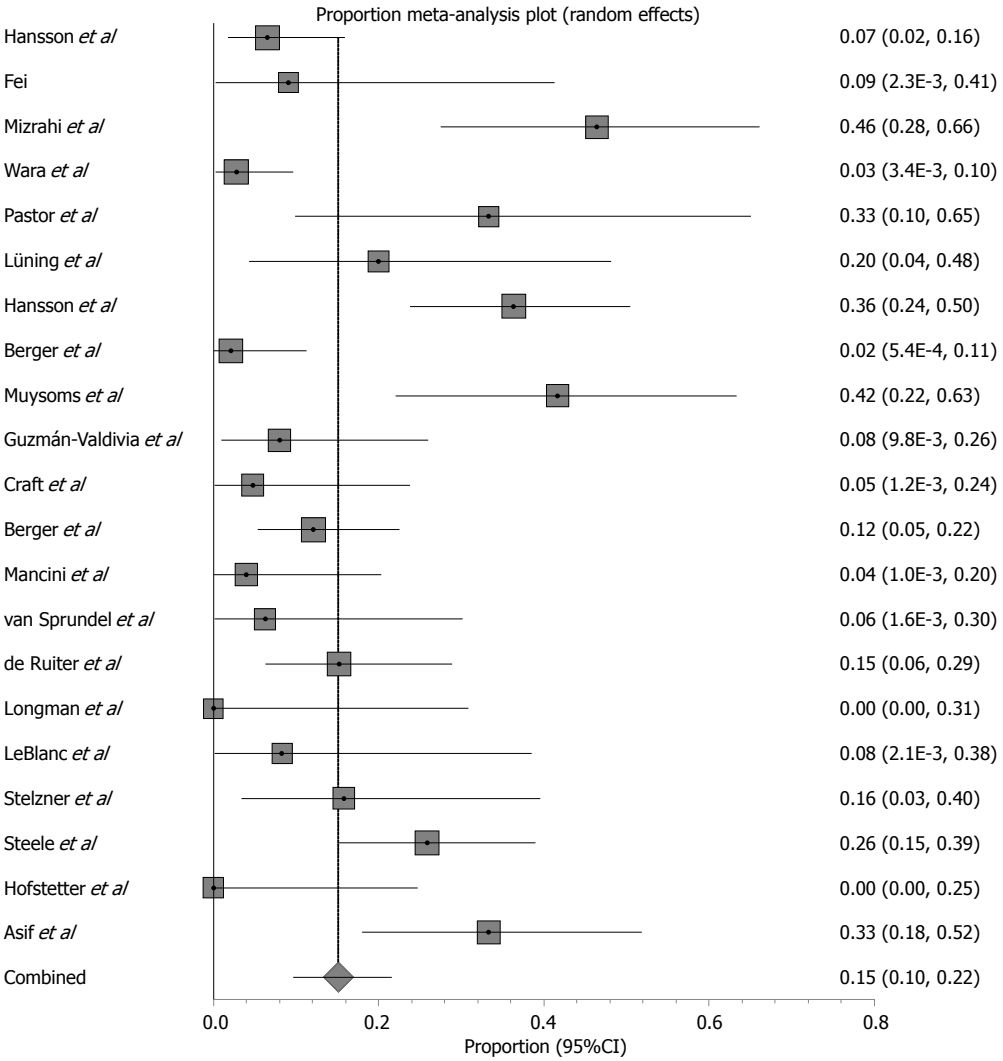

Figure 5 Proportion of hernia recurrences after synthetic mesh repair of parastomal hernia. The square shape represents the weight of the study, and the horizontal line through the square represents the confidence interval of the effect estimate (random-effects model; Cochran's *Q* test = 90.8; I^2 = 78%; $P \leqslant 0.0001$).

hernia recurrence, synthetic mesh repair resulted in a significantly lower rate compared to biologic mesh repair (OR = 1.96; 95%CI: 1.16-3.30; *P* = 0.01). No significant difference was found concerning wound infection (OR = 1.76; 95%CI: 0.58-5.38; *P* = 0.32), mesh infection (OR = 0.29; 95%CI: 0.02-4.83; *P* = 0.39) or other complications (OR = 0.59; 95%CI: 0.29-1.22; *P* = 0.15) (Table 4).

Anatomic position of the prosthesis

Various mesh positions were applied concerning biologic mesh repair, including inlay, onlay, sublay and underlay (intraperitoneal) placement of the mesh. Two retrospective series reported on 40 cases that involved onlay mesh repairs. Hernias recurred in 31.3% (weighted pooled proportion, 95%CI: 0.9-78.8) of patients. Smart *et al*[4] placed 16 stomas lateral to the rectus sheath, which showed a high recurrence rate (75%) compared to 11 stomas within the rectus sheath (27%)[4,24]. Ellis *et al*[19] placed the mesh intraperitoneally using the Sugarbaker technique. Two of 20 (10%) patients had a recurrent hernia after a

Table 5 Summary of pooled proportions of outcome measures of open synthetic mesh repair *vs* laparoscopic synthetic mesh repair

Hernia repair	No. of studies	No. of mesh repairs	Recurrence	Complications		
				Wound infection	Mesh infection	Other
Open repair	9	213	13.5% (8.1-20.2)	3% (1.2-5.7) FE	2.3% (0.7-4.8) FE	12.8% (7.4-19.4)
Laparoscopic repair	10	397	18% (8.9-29.5)	2.4% (0.804.8) FE	3.6% (1.9-5.7) FE	23.8% (14.5-34.6)
P value			0.37	0.79	0.5	⩽ 0.0001

FE: Fixed-effect model.

follow-up of 18 mo. The sandwich technique, which combines the onlay and sublay technique, was reported by Taner *et al*[25]. After a mean follow-up of 10 mo, two of 13 (15%) patients had a recurrent hernia. One other study reported multiple surgical techniques (including inlay and onlay) and did not allow for stratified outcome extraction[18]. Considering the anatomical position for open synthetic mesh repair, 3 retrospective studies using a series of onlay synthetic mesh repairs, reporting a total of 119 repairs, were included in this study. Hernias recurred in 21.5% (weighted pooled proportion, 95%CI: 14.7-29.3) of patients. In three studies, the mesh was placed in the sublay position, and 3 hernia recurrences with a weighted-pooled proportion of 8.1% (95%CI: 2.1-17.4) were reported.

The mesh was placed intraperitoneally by the open approach in three studies reporting 48 repairs (19 Sugarbaker and 29 keyhole technique repairs)[36-38]. The weighted-pooled proportion of recurrence was 8.8% (95%CI: 1.8-20.2). Seven studies described laparoscopic synthetic mesh repair using the Sugarbaker technique, and the weighted-pooled proportion of hernia recurrence was 10.9% (95%CI: 3.7-21.4). The keyhole technique was used in 8 studies, and hernia recurrence was reported in 35.6% (weighted pooled proportion; 95%CI: 14.6-60.1).

Surgical approach

All biologic mesh repairs were *via* the open approach. Considering the surgical approach used for synthetic mesh repair, 9 studies reported open repairs, 10 studies reported laparoscopic repairs, and 2 studies reported combined open and laparoscopic repairs. Unfortunately, separate data of the different approaches in these last two studies could not be extracted. Within the nine studies that reported 213 open synthetic mesh repairs, hernias recurred in 13.5% (weighted pooled proportion; 95%CI: 8.1-20.2) of patients. Wound infection, mesh infection and other complications were reported in 3% (95%CI: 1.2-5.7), 2.3% (0.7-4.8) and 12.8% (95%CI: 7.4-19.4) of the cases, respectively. Ten studies reported 397 laparoscopic synthetic mesh repairs. The weighted-pooled proportion of hernia recurrence was 18% (95%CI: 8.9-29.5). Wound infection, mesh infection and other complications were reported in 2.4% (95%CI: 0.8-4.8), 3.6% (95%CI: 1.9-5.7) and 23.8% (95%CI: 14.5-34.6) of the cases, respectively.

Comparison of surgical approach: Comparing open *vs* laparoscopic mesh repair did not result in a significant difference in hernia recurrence (OR = 0.81; 95%CI: 0.51-1.28; *P* = 0.37), wound infection (OR = 1.17; 95%CI: 0.38-3.62; *P* = 0.79) or mesh infection (OR = 0.67; 95%CI: 0.21-2.14; *P* = 0.50). A significantly (OR = 0.39; 95%CI: 0.25-0.63; *P* ⩽ 0.0001) lower occurrence rate of other complications was observed with open repair (Table 5). Regarding laparoscopic synthetic mesh repair, the Sugarbaker technique resulted in a significantly lower recurrence rate of parastomal hernia compared to the keyhole technique (OR = 0.35; 95%CI: 0.21-0.59; *P* ⩽ 0.0001).

Prophylactic mesh placement

Eighteen studies reported a total of 500 prophylactic mesh placements, which included 13 studies consisting of 382 patients with synthetic mesh repair and 5 studies consisting of 118 patients with biologic mesh repair. The follow-up ranged from 7-65 mo.

The overall mortality was 2.5% (21 deaths, weighted pooled proportion, 95%CI: 1.3-4.2) None of the deaths were related to the mesh. Two postoperative deaths were due to progressive metastatic disease, one was due to a pulmonary thromboembolism, and two were due to cardiopulmonary complications[22,23,39-41]. Jänes *et al*[42] reported five deaths due to septic or cardiovascular complications not further specified. Fleshman *et al*[20] described eleven deaths, none of which were related to the device or treatment not further specified.

Study characteristics and outcomes, including weighted-pooled rates of hernia occurrence and wound-related complications, are shown in Table 6. When comparing prophylactic placement of biologic mesh with synthetic mesh, there was no significant difference in hernia occurrence (OR = 0.79, 95%CI: 0.40-1.55; *P* = 0.49) or wound infection (OR = 0.30, 95%CI: 0.07-1.28; *P* = 0.10). In the mesh group, 58 hernia occurrences were observed with a weighted-pooled proportion of 11.5% (95%CI: 7.1-16.8) (Figure 6) and 31 wound infections with a weighted-pooled proportion of 6.9% (95%CI: 3.6-11.1), and no infections of the prosthesis were reported [0% (95%CI: 0-2.0)].

From the 15 studies reporting hernia occurrence, 9 elaborated on treatment received. Five studies reported 21 reoperations because of a symptomatic hernia not further specified[6,20,23,40,43]. Two studies reported 5

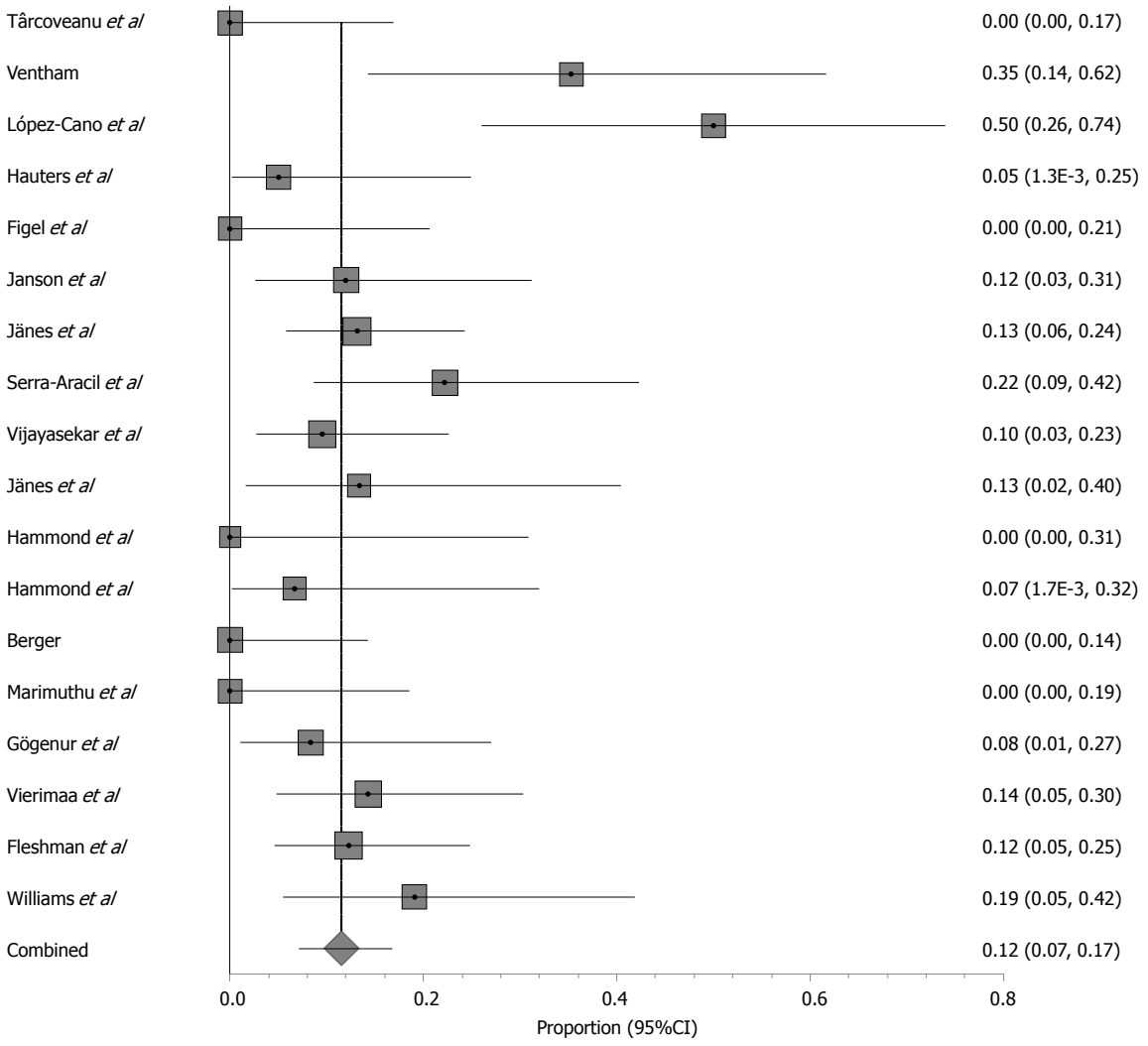

Figure 6 Proportion of hernia occurrence after prophylactic mesh placement. The square shape represents the weight of the study, and the horizontal line through the square represents the confidence interval of the effect estimate (random-effects model; Cochran's *Q* test = 45.5; I^2 = 62.7%; *P* = 0.0002).

patients who underwent reoperation involving relocation of stoma and mesh repairs[44,45]. All other reported hernia occurrences were asymptomatic and treated conservatively[6,16,22,45]. Six studies reported treatment of a wound infection[6,22,39,42,45,46]. Sixteen patients were treated conservatively, 7 patients were treated by surgical drainage, and 2 patients were treated with systemic antibiotics. Other complications were seroma (7%), cardiopulmonary event (4.7%), urinary tract infection (5.4%), cutaneous/fascial dehiscence (3.9%), stoma necrosis (12.4%), intra-abdominal/pelvic infection (1.6%) stoma-related problems (1.6%), miscellaneous (20.9%) and severe events not further specified (39.5%). All nine reported seromas were treated by surgical drainage[44].

Meta-analysis was performed on the data concerning the incidence of parastomal hernia in the seven randomized controlled trials (Figure 2). Overall, parastomal hernias occurred significantly less in the prophylactic group (weighted-pooled proportion 14.9%; 95%CI: 6.1-26.6) compared to the conventional stoma group (46.8%; 95%CI: 24.7-69.7) (OR = 0.20; 95%CI: 0.08-0.50; *P* = 0.0006). Concerning the use of prophylactic biologic mesh repair or synthetic mesh repair, there was no significant difference in parastomal hernia occurrence (OR = 0.48; 95%CI: 0.18-1.25; *P* = 0.13). Additionally, there was no significant difference found between both groups (7.8%; 95%CI: 1.8-17.5 *vs* 8.2%; 95%CI: 4.2-13.4) regarding wound infection (OR = 1.04 95%CI: 0.53-2.02; *P* = 0.91 FE).

Anatomic position of the prosthesis: Considering the surgical technique used for prophylactic mesh repair, 12 studies reported open reinforcement, and 3 studies reported laparoscopic reinforcement. Unfortunately, separate data of 2 studies combining open and laparoscopic reinforcement and 1 study combining the onlay and sublay techniques did not allow for stratification of outcomes.

Williams *et al*[41] used the stapled mesh stoma reinforcement technique (SMART) and reported 21 prophylactic mesh placements and 4 hernia occurrences.

In eleven studies, of which ten reported open and

Table 6 Study characteristics and outcomes of prophylactic mesh placement of parastomal hernia *n* (%)

Ref.	No. Patients (completed follow-up)		Type of stoma	Material; technique	Parastomal hernia[1]		Wound infection		Mesh infection	Other[3]		Mortality	Follow-up (mo)
	Mesh	No mesh			Mesh	No mesh	Mesh	No mesh	Mesh	Mesh	No mesh		
Târcoveanu *et al*[44]	20	22	C: 42	O: 42; Sublay; PP	0	6 (27)	0	2 (9)	0	9 (45)	11 (50)	0	9 (median)
Ventham *et al*[63]	17	24	C: 42	O: 42; Sublay; PP	6 (35)	13 (54)	2 (12%)	1 (4)	NS	0	0	0	12
López-Cano *et al*[40]	19 (18)	17 (16)	C: 36	L: 36; IPOM; SB; Proceed	9 (50)	15 (94)	8 (44)	3 (19)	0	16 (89)	5 (31)	1[2] (3)	12
Hauters *et al*[16]	20	-	C: 20	L: 17 O: 3; IPOM; SB: 20; PCM	1 (5)	-	0	-	0	6 (30)	-	0	24
Figel *et al*[62]	16	-	C: 16	O: 16; IPOM; SB: 12; K: 4; Surgisis	0	-	0	-	0	NS	-	0	38 (median)
Janson *et al*[64]	25	-	C: 25	L: 25; Sublay; ULTRAPRO	3 (15)	-	2 (8)	-	0	1 (4)	-	0	19
Jänes *et al*[42]	75 (61)	18 (12)	C: 79 I: 14	O: 93; Sublay; ULTRAPRO	8 (13)	8 (67)	6 (8)	4 (22)	0	0	0	5[2] (5)	15
Serra-Aracil *et al*[6]	27	27	C: 54	O: 54; Sublay; ULTRAPRO	6 (22)	12 (44)	4 (15)	4 (15)	0	1 (4)	1 (4)	0	29
Vijayasekar *et al*[45]	42	-	C: 33 I: 9	O: 42; Sublay; PP	4 (10)	-	1 (2)	-	0	1 (2)	-	0	31
Jänes *et al*[43]	27 (15)	27 (21)	C:54	O: 54; Sublay; Vypro	2 (13)	17 (81)	0	0	0	0	0	0	65
Hammond *et al*[68]	10	10	NS	O: 20; Sublay; Permacol	0	3 (30)	0	0	0	0	0	0	6.5
Hammond *et al*[21]	15	-	NS	O: 15; Onlay: 6; Sublay 9; Permacol	1 (7)	-	NS	-	NS	NS	-	0	7 (median)
Berger[39]	25 (24)	-	C: 24 I: 1	L: 6, O: 19; IPOM; K; DynaMesh	0	-	0	-	0	0	-	1[2] (4)	11
Marimuthu *et al*[46]	18	-	NS	O: 18; Sublay; Surgipro	0	-	1 (6)	-	0	1 (6)	-	0	16
Gögenur *et al*[22]	25 (24)	-	C: 25	O: 25; Sublay; StomaMesh	2 (8)	-	4 (17)	-	0	6 (25)	-	1[2] (4)	12
Vierimaa *et al*[23]	42 (35)	41 (32)	C: 83	L: 83; IPOM; K; DynaMesh	5 (14)	12 (38)	1 (3)	2 (6)	NS	9 (21)	10 (24)	1[2] (1)	12
Fleshman *et al*[20]	55 (49)	58 (53)	C: I:23/ C:35 I: I:19/ C:36	O: 113; Sublay; STRATTICE	6 (12)	7 (136)	2 (4)	3 (6)	0	21 (38)	30 (52)	11[2] (10)	24
Williams *et al*[41]	22 (21)	11	C: I:4/ C:7 I: I:11/ C:11	I: O = 18 L = 4 C: O = 11 SMART Onlay; Permacol	4 (19)	8 (73)	NS	NS	0	2 (9)	0	1[2] (3)	I: 18 C: 9
Weighted pooled %; (95%CI)					11.5% (7.1-16.8)	51.5% (33.7-69.1)	6.90% (3.6-11.1)	9.30% (4.8-15.1)	0% (0-2.0) FE	14.20% (5.5-26.0)	13.80% (3.0-30.7)	2.6% (1.3-4.4)	

[1]With regard to lost after follow-up; [2]Unrelated to mesh; [3]Seroma 9 (10); Cardiopulmonary event 6 (10, 436); Urinary tract infection 7 (10, 436); Cutaneous/fascial dehiscence 5 (53, 231,436); Stoma (mucosal/intestinal) necrosis 16 (53, 126, 163, 173, 227,436); Intra-abdominal/pelvic infection 2 (436, 489); Intestinal occlusion 4 (436,489); Stoma-related problems 2 (436); Other 27 (10, 53, 54, 231); Severe events not further specified 51 (488). L: Laparoscopic; O: Open; C: Colostomy; I: Ileostomy; SB: Sugarbaker; PP: Polypropylene mesh; IPOM: Intraperitoneal mesh; PCM: Parietex composite mesh; SMART: Stapled mesh stoma reinforcement technique.

one reported laparoscopic reinforcements, the mesh was placed in the sublay position, and 37 hernia occurrences with a weighted pooled proportion of 11.5% (95%CI: 6.9%-17.1%) were reported. The mesh was placed intraperitoneally in three studies. Figel *et al*[62] used the open intraperitoneal surgical technique and reported 16 stoma reinforcements without hernia occurrences. Two studies reported the laparoscopic surgical reinforcement technique. Lopez-Cano *et al*[40] used the Sugarbaker technique and reported 18 mesh placements and 9 (50%) hernia occurences. Vierimaa *et al*[23] used the keyhole technique and reported 35 mesh placements and 5 (14%) hernia occurrences.

DISCUSSION

The current study evaluated and compared all the evidence regarding the use of biologic and synthetic mesh for repair and prevention of parastomal hernia. Interestingly, the results of comparing biologic and synthetic mesh repairs showed a comparable or even superior result regarding parastomal hernia recurrence (24% *vs* 15.1%) and wound infection (5.6% *vs* 2.8%) in favour of the synthetic mesh repair. Overall, the mesh infection rate was low. Only sixteen mesh infections were reported in 753 repairs (2.1%), which resulted in fourteen mesh removals (all synthetic meshes). However, these observations should be interpreted cautiously because of the low to moderate quality of the studies.

Biologic mesh has gained widespread popularity in the context of infection and a contaminated environment because of their proposed advantages, including biocompatibility resulting in rapid vascularization and migration of host (immune) cells. It is thought that biologic prostheses are therefore less susceptible to infection than their synthetic counterparts. The ventral hernia working group regards parastomal hernia repair as potentially contaminated (grade 3) and therefore recommends biologic mesh repair[47]. Many authors believe that synthetic mesh should not be used in a contaminated environment or in close proximity to the bowel and stoma due to the risk of erosion and fistula formation. However, studies with high-level evidence are lacking, and the exact origins of these concerns are difficult to identify, are mostly anecdotal or reference old reports using inferior materials and techniques[48-50]. Primus and Harris criticized the surgical literature on the use of biologics in contaminated fields, arguing that cumulative data do not support the claim that biologics are indicated for use in contaminated fields. The primary literature varies widely in terms of sample size, diagnosis of (recurrent) PSH, methods of mesh placement, follow-up period, reported hernia recurrences and surgical site infection[51]. Rosen *et al*[52] reported a critical review of the surgical literature on biologic mesh repair, which revealed that the majority of the studies evaluating the outcomes of biologic mesh are actually reporting the repair of clean defects. This finding is very surprising given the high costs of biologic mesh, whereas the position of synthetic mesh in "clean" hernia repair has been proven. Despite the lack of high-grade evidence, biologic meshes are still preferred above synthetic mesh in contaminated fields as noted by Bondre *et al*[53], who conducted a multicentre study about practice patterns in contaminated ventral hernia repair. This review shows a comparable to superior result of synthetic mesh over biologic mesh concerning parastomal hernia recurrence. This finding is confirmed by Lee *et al*[54] in a systematic review on ventral hernia mesh repair in contaminated fields. Mesh removal due to infection is a much-feared complication. The literature suggest that biologic mesh does not prevent infection but can be more easily salvaged when infection arises[55]. This review challenges the concept that contaminated hernias should be repaired with expensive biologic mesh. Only sixteen mesh infections were seen in this current review, resulting in mesh removal from 14 patients. Concerning parastomal hernia repair, surgeons should carefully balance the risks and costs with the benefits when deciding on the choice of mesh for parastomal hernia repair.

Similar to ventral hernia repair, the prosthesis is placed in either the inlay, onlay, sublay, or underlay (intraperitoneal) position during parastomal hernia repair. None of the included studies used an inlay placement of the prosthesis. Onlay mesh repair showed the highest recurrence rate, whereas the sublay technique showed the lowest in the current study. There was no difference in wound and mesh infection rates between the various anatomic positions. However, firm conclusions cannot be drawn based on this subanalysis because these results were obtained from small groups. Each method of mesh repair has its own theoretical advantages and disadvantages. Laparotomy is avoided with the onlay technique, but it requires extensive dissection of subcutaneous tissue, which predisposes patients for haematoma and seroma formation. Disruption of skin vascularization may lead to impaired wound healing. Additionally, intra-abdominal pressure may lead to lateral detachment of the prosthesis, resulting in the higher recurrence rates. The sublay mesh technique protects the mesh from bacterial contamination while minimizing contact with the bowel because the mesh is enveloped in well-vascularized tissue, whereas the fascia and peritoneum form a natural barrier between prosthesis and abdominal organs. This technique reduces the risk of infection, adhesion or fistulation. The anatomic positions of the sublay and intraperitoneal mesh technique are more attractive because of the benefits from intra-abdominal pressures, which help to keep the mesh in place.

Concerning laparoscopic *vs* open parastomal hernia repair, this review shows similar results regarding hernia recurrence (18% *vs* 13.5%; $P = 0.37$), wound infection (2.4% *vs* 3%; $P = 0.79$) and mesh infection (3.6% *vs* 2.3%; $P = 0.50$). However, a significantly lower rate of other complications was seen with open repair

(23.8% *vs* 12.8%; $P < 0.0001$), which was mostly due to the high occurrence of seroma formation in three laparoscopic repair studies[5,8,31].

When performing laparoscopic intraperitoneal repair there was a significantly lower recurrence rate of parastomal hernia using the Sugarbaker technique compared to the keyhole technique (10.9% *vs* 35.6%, OR = 0.35; 95%CI: 0.21-0.59; $P \leqslant 0.0001$). Remarkably, it appears that all failures using the keyhole technique were related to the use of an e-PTFE-mesh. As noted by Hansson *et al*[9], using the keyhole technique estimation of the size of the hole is difficult as mesh shrinkage may result in enlargement of the central hole and reherniation.

Unfortunately, the recurrence rate is still up to one third after mesh repair of parastomal hernias. Our systematic review with meta-analysis shows that prevention of parastomal hernia by the use of mesh at the time of stoma formation reduces the incidence of parastomal hernia significantly compared to the conventional stoma group (14.9% *vs* 46.8% OR = 0.20; 95%CI: 0.08-0.50; $P \leqslant 0.0006$). Interestingly, placement of preventive mesh did not result in increased wound infection or mesh infection. Recently published reviews also confirm our conclusion that prophylactic insertion of a mesh when forming a stoma prevents parastomal hernia without increasing the incidence of wound infections or other mesh-related complications[56,57].

One point of discussion remains whether universal reinforcement is expedient and cost-effective. Other non-mesh prophylactic measures can be considered, such as lateral rectus abdominis positioned or extra-peritoneal positioned stomas[58,59]. Most patients who develop a parastomal hernia are asymptomatic. However, complications due to an untreated parastomal hernia (incarceration, obstruction, strangulation) can be severe and are associated with significant morbidity and mortality. Identification of patients in whom reinforcement is beneficial is essential as the patient can avoid unnecessary longer operative time, costs and possible long-term complications associated with mesh placement. As noted by Hotouras *et al*[60], risk factors for parastomal hernia formation include abdominal obesity, increasing age, corticosteroid use, poor nutritional status, increased intra-abdominal pressure, connective tissue disorders and other disorders that predispose patients to wound infection such as diabetes. Factors that need to be considered include the reason for the stoma (temporary or permanent stoma), patient co-morbidity, chance of reoperations and risk factors concerning parastomal hernia formation. Patients undergoing stoma formation with short life expectancies will often not survive long enough to develop a parastomal hernia, and patients who are healthy enough to undergo stoma reversal before hernia occurrence would not benefit from prophylactic mesh placement.

Median direct costs for complex ventral hernia repairs with biologic mesh ($16970) is more than twice the amount compared to repairs with synthetic mesh ($7590)[61]. Parastomal hernia repair probably costs less due to the need for smaller meshes; however, a substantial cost difference is expected to remain. Figel *et al*[62] calculated that by using a bio-prosthetic and considering a 30% incidence of surgical management of parastomal hernia repair, it would be cost-effective if the prosthesis cost less than $4312. The decision to place prophylactic mesh after stoma formation must be patient tailored and may certainly be justified in selected patients. However, standard application in all patients does not seem warranted. More randomized controlled trials with adequate power for risk stratification and subsequent costs of usage of biologic and synthetic mesh are needed.

Most of the studies that were included are retrospective cohorts (level 3 evidence), which could introduce selection and information bias and are affected by heterogeneity. Most study populations were diverse with different types of stomas and indications for the initial surgery. The high recurrence rate regarding biologic parastomal mesh repairs was mostly determined by one study: A 75% recurrence rate of 16 stoma repairs lateral to the rectus sheath compared to a 27% rate when the repair was within the rectus sheath. As noted by Smart *et al*[4], parastomal hernia repairs where the stoma is lateral to the rectus sheath had a significantly higher risk of recurrence and suggested that this higher risk was likely due to the inherent strength of the tissue onto which the onlay mesh was sutured.

Unfortunately, reporting was insufficient to allow proper stratification for individual risk factors for parastomal hernia. Follow-up time and diagnostic modalities used for determining recurrence rates had a strong impact on the outcome. The longer the follow-up period was, the more recurrences were found. In addition, the diagnostic modalities differ in terms of sensitivity and specificity. Some recurrences found may be of no clinical relevance. Reported follow-up periods within and between studies varied from 7 mo to 51 mo. As recurrence occurs mostly in the first years after operation a minimum follow up of 12 mo seems appropriate.

Definitions of parastomal hernia, wound infection and mesh infection were ill-defined in most studies, and the modality of determining hernia recurrence (*e.g.*, clinical evaluation or CT imaging) was often not clearly stated. Therefore, the results of this review should be interpreted with care.

In an effort to reduce the effect of low quality studies, we excluded the high risk of bias randomized controlled trials for the prophylactic mesh meta-analysis. Only three studies considered of sufficient methodological quality remained, and a second meta-analysis was performed[20,23,40]. No significant difference was found in the occurrence of parastomal hernia when comparing the prophylactic group to the conventional

group (OR = 0.33; 95%CI: 0.09-1.20; *P* = 0.09).

However, provided the large amount of parastomal hernia repairs included in the current report, meaningful conclusions may be drawn regarding optimal surgical management of synthetic and biologic mesh repair in parastomal hernia recurrence.

Clinical implications

The current evidence suggests there is no superiority of (more expensive) biologic mesh over synthetic mesh for parastomal hernia repairs after parastomal hernia recurrence, wound infection and mesh infection. In the context of cost-effective healthcare, careful consideration must be taken in choosing the types of materials to use[55]. Sublay seemed to be the most advantageous anatomic position of the mesh, as this position resulted in the lowest recurrence and protects the mesh from bacterial contamination while minimizing contact with the bowel. No difference was found for parastomal hernia recurrence between open or laparoscopic parastomal hernia repairs. When performing laparoscopic repair, the keyhole technique should be abandoned in favour of the Sugarbaker technique when using an ePTFE-mesh because of much higher recurrence rates. As shown by Wara *et al*[5], the keyhole technique can be considered when using a polypropylene-based mesh or with open parastomal keyhole hernia repairs.

Prophylactic mesh placement at the initial surgery significantly reduced parastomal hernia occurrence on the mid-long term without increasing wound infection or mesh infection. However, it has yet to become clear what the long-term results will be. The number of recurrences will increase over time, though at a slower pace than in the first few years after mesh placement. The same applies to some specific long-term side effects such as mesh infection and mesh-related fistulas. Although their incidence may be low, their impact is disproportionately high.

Identification of patients in whom reinforcement is mandatory is essential, as the patient can avoid unnecessary longer operative time, costs and possible long-term complications associated with mesh placement.

Altogether there is still not enough evidence to recommend the use a biologic mesh over synthetic mesh under contaminated conditions in general and specifically not for parastomal hernia repair. Prophylactic mesh reinforcement during stoma formation significantly reduces parastomal hernia occurrence regardless of mesh type. Yet, a significant number of patients will develop asymptomatic parastomal hernia and there are no data on long term effects of preventive mesh placement. Therefore, it is essential to select the right patient for whom prophylactic reinforcement is mandatory.

COMMENTS

Background

Parastomal hernia develops in 50% of patients. Hernias are often asymptomatic and managed with conservative treatments; however, 11% to 70% of patients undergo surgery due to discomfort, pain, obstructive symptoms and cosmetic dissatisfaction. Although standard care is mesh repair, prevention by prophylactic mesh placement is gaining popularity. The use of biologic mesh is becoming more popular as it claims less infections with sustained durability of the repair compared to synthetic mesh. The primary aim of the current study was to compare biologic and synthetic mesh use for the treatment and prevention of parastomal hernia by systematic review and meta-analysis of available data in the literature. The secondary aim was to evaluate different anatomical positions and surgical techniques concerning parastomal hernia repair.

Research frontiers

The recurrence rate of parastomal hernia is the lowest after mesh repair (0%-33%), whereas primary fascial closure (46%-100%) and relocation of the stoma (0%-76%) result in much higher rates. Although low recurrence rates are reported after synthetic mesh repair, concerns have been raised regarding the safety of synthetic meshes in (potentially) contaminated fields due to the risk of mesh infection and subsequent removal.

Innovations and breakthroughs

Biologic mesh was first introduced in the 1980s and was developed with the concept that due to its bio-degradable nature, it has the potential to ameliorate problems in infected and contaminated fields. No clear answer can be given as to whether there is a difference in the clinical outcomes between synthetic and biologic mesh repairs. The high prevalence of parastomal hernia and difficulty of repair have led to a shift of focus from repair towards prevention using prophylactic mesh reinforcement at the time of stoma formation.

Applications

This review and meta-analysis suggests there is no superiority of biologic over synthetic mesh for parastomal hernia repair after parastomal hernia recurrence, wound infection and mesh infection. Prophylactic mesh reinforcement during stoma formation significantly reduces parastomal hernia occurrence regardless of the mesh type. Identification of patients for whom reinforcement is mandatory is essential, and mesh reinforcement should be reserved for selected patients.

Terminology

Ostomy formation requires the creation of a full-thickness defect within the abdominal wall. Parastomal hernia is a type of incisional hernia that allows protrusion of abdominal contents through an abdominal wall defect that is created. Both synthetic mesh and biologic mesh (acellular collagen matrix) are used in parastomal hernia repair. There are various approaches regarding the anatomic position of the mesh during parastomal hernia repair. Meshes can be implanted in an inlay (between the fascia), onlay (over the fascia), sublay (below the anterior fascia and muscular level but above peritoneum) or underlay (intraperitoneal) position. Laparoscopic repair involves the intraperitoneal technique, and open repair may involve any of the anatomical planes of the mesh. When performing intraperitoneal repair, the choice can be made between the Sugarbaker and keyhole repair technique.

Peer-review

In this systematic review, the authors have presented a thorough and critical analysis of biologic and synthetic mesh use for the treatment and prevention of parastomal hernias. With a focus on hernia recurrence in the absence of rigorous data in the literature, the current review contributes to the increased understanding of parastomal hernias.

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META-ANALYSIS

Complete revascularization reduces adverse outcomes in patients with multivessel coronary artery disease

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Abstract

AIM

To investigate the influence of complete and incomplete revascularization (ICR) in patients with multivessel coronary artery disease undergoing coronary artery bypass or percutaneous coronary intervention.

METHODS

We searched PubMed using the keywords "complete revascularization", "incomplete revascularization", "coronary artery bypass", and "percutaneous coronary intervention". We selected randomized controlled studies (RCT) and observational studies only for review. The main outcomes of interest were mortality, myocardial infarction (MI) and repeat revascularization. We identified further studies by hand searching relevant publications and included those that met with the inclusion criteria in our final analysis and performed a systematic review.

RESULTS

Ten studies were identified, including 13327 patients of whom, 8053 received complete revascularization and 5274 received ICR. Relative to ICR, CR was associated with lower mortality (RR: 0.755, 95%CI: 0.66 to 0.864, P = 0.765, I^2 = 0.0%), lower rates of MI (RR: 0.759, 95%CI: 0.615 to 0.937, P = 0.091, I^2 = 45.1%), lower rates of MACCE (RR: 0.731, 95%CI: 0.668 to 0.8, P = 0.453, I^2 = 0.0%) and reduced rates of repeat coronary revascularization (RR: 0.691, 95%CI: 0.541 to 0.883, P = 0.0, I^2 = 88.3%).

CONCLUSION

CR is associated with lower rates of adverse outcomes. CR can be used as a standard in the choice of any particular revascularization strategy.

Key words: Complete revascularization; Percutaneous coronary intervention; Coronary artery bypass grafting;

Incomplete revascularization

Core tip: Completeness of revascularization has been documented to have lesser adverse post-operative/post-procedural outcomes as compared to incomplete revascularization (ICR). We conduct a systematic review with meta-analysis to analyze the outcomes in patients undergoing CR *vs* ICR, using any or both techniques. Ten studies were identified, including 13327 patients of whom, 8053 received CR and 5274 received ICR. CR is associated with lower rates of mortality, MI, repeat coronary revascularization procedures, and MACCE. Subgroup analysis also showed reduced rates of adverse events. CR can be used as an aim for any myocardial revascularization procedure.

Auchoybur ML, Chen X. Complete revascularization reduces adverse outcomes in patients with multivessel coronary artery disease. *World J Meta-Anal* 2017; 5(6): 167-176 Available from: URL: http://www.wjgnet.com/2308-3840/full/v5/i6/167.htm DOI: http://dx.doi.org/10.13105/wjma.v5.i6.167

INTRODUCTION

Complete revascularization arose from early studies on coronary artery bypass grafting (CABG) surgery whereby some studies demonstrated that patients who were completely revascularized enjoyed a mortality benefit over those who were incompletely revascularized[1-3]. Data from the coronary artery surgery study (CASS) registry show that patients with multi-vessel coronary artery disease (CAD) and severe angina that received three or more grafts had better survival relative to patients who received one or two grafts[4]. Although CR is often easier to achieve with CABG than with percutaneous coronary intervention (PCI), with recent developments in percutaneous transluminal coronary angioplasty procedures, such as the new era of drug eluting stents (DES), the previous barriers of PCI in the treatment of multi-vessel disease are no longer insurmountable, and favorable outcomes have been recorded across multiple centers using this revascularization approach[5].

Different established standards are used to determine the degree of completeness of revascularization. Conventionally, perfusion districts are divided into three areas according to the supply of the coronary artery branches namely the left anterior descending (LAD), the left circumflex (LCX) and the right coronary artery (RCA). The most commonly used definition across studies is the (1) anatomical definition, and was used in 90% of the studies included in our meta-analysis. According to this definition, CR has been achieved if all diseased arterial segments with a vessel size (greater/equal to 1.5 mm for a graft and 2.0-2.25 mm for a stent) with at least one significant stenosis greater than or equal to 50% receive a graft or a stent. A second definition of CR is (2) numerical whereby the number of distal anastomoses is greater or equal to the number of diseased coronary segments/systems and was used in 10% of the studies included in our meta-analysis. Other definitions include the (3) functional definition whereby all ischemic myocardial territories are grafted (or stented); areas of old infarction with no viable myocardium are not required to be perfused, the (4) score-based definition whereby the stenosis in different vessels is scored and different weights are given to different vessels according to number of myocardial segments supplied (A residual score of 0 is usually considered equivalent to CR) and the (5) physiology-based definition whereby all coronary lesions with fractional flow reserve of less than equal to 0.75-0.80 receive a graft or stent.

Due to procedural difficulties associated with each technique (CABG and PCI), complete revascularization is not always achieved. Previous studies have tried to assess the outcomes following incomplete revascularization (ICR). However, since there is no specific definition for ICR, which is essentially defined as "failure to achieve complete revascularization", it lacks objectivity as it relies on post-procedural classification of CR by the treating surgeon/physician. The SYNTAX trial, which used a more accurate method to determine the completeness of revascularization (patients were categorized as incompletely revascularized when the number of diseased segments that were treated did not match the heart team decision), and the BARI trial reported no increase in adverse outcomes in incompletely revascularized patients.

There is discrepancy between the results of different studies concerning the superiority of CR over ICR. In our meta-analysis, we aim to determine whether CR, is associated with improved post-procedural outcomes. In a subgroup analysis, we also investigate the mid/long-term outcomes of CR, along with outcomes in a > 60 years old patient population.

MATERIALS AND METHODS

We identified four types of studies on the PubMed database: Randomized controlled trials, observational studies, controlled clinical trials and clinical trials. The study was conducted in March 2016, using the keywords "coronary artery bypass", "percutaneous coronary intervention", "complete revascularization", "incomplete revascularization". The total number of records identified was fifty-four. We limited our search to the specific above-mentioned study types. Six of these studies met with our inclusion criteria. Through Hand-search (a methodological approach previously validated), we searched through journals related to our subject-matter and identified relevant studies and also searched the latter's references. An additional four manuscripts were selected using the above-mentioned method[6]. A total of

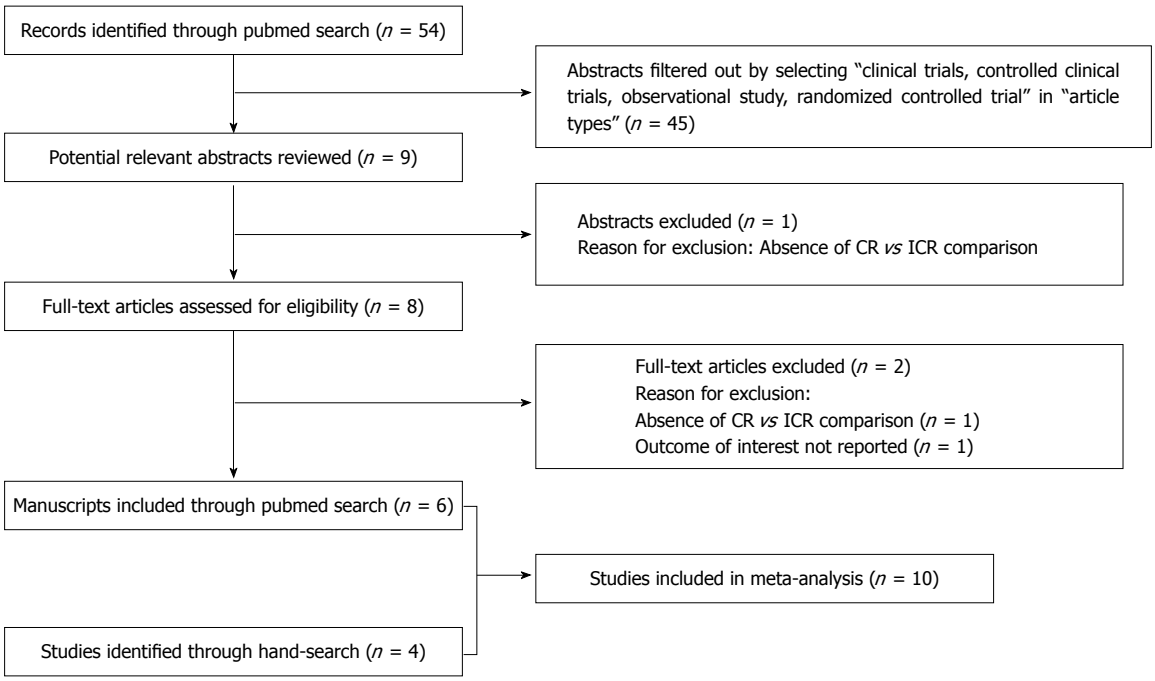

Figure 1 Flow diagram of literature search and study selection. ICR: Incomplete revascularization.

ten studies were included in our final analysis.

Data sources and study search strategy

We included two types of studies in our meta-analysis, namely randomized controlled trials and observational studies in which: (1) Patients with multi-vessel CAD were enrolled for either CABG or PCI; (2) the outcomes of interest between CR and ICR were compared using any of the definitions of CR (see introduction for definitions of CR used); and (3) the outcomes included the primary outcome of interest and/or the secondary outcomes. We excluded studies in which: (1) multiple grafts were used for treatment of multi-vessel CAD without any reference to CR and/or ICR; (2) PCI was used for the treatment in the setting of ST-elevation acute myocardial infarction (MI); (3) outcomes of interest were not reported unless there was reference to CR and ICR; (4) the patients included were undergoing repeat CABG surgery; and (5) the sample size was small (< 100 patients).

Study selection

Our initial search using the keywords: Complete revascularization, ICR, coronary artery bypass, PCI yielded fifty-four citations on PubMed. Using the filter for article types, we selected clinical trials, controlled clinical trials, observational studies and randomized controlled trials only. Of the fifty-four citations, nine citations remained, and the abstracts from these nine citations were reviewed. Of these, one abstract was excluded due to absence of comparison between complete and ICR. The remaining eight full text manuscripts were reviewed for eligibility. Of these eight manuscripts, six met with our inclusion criteria. We hand-searched references cited in relevant publications and an additional four manuscripts that fit our inclusion criteria were included. A total of ten studies were selected and included in this meta-analysis (Figure 1).

Data extraction

The data was extracted by Merveesh L Auchoybur using standardized extraction forms. Extracted information included study design, method of revascularization and definition of CR used by each study, follow-up time, patient characteristics pre-operatively, and outcomes relevant to this meta-analysis. The subjects were divided into two groups, namely the complete revascularization group for those subjects who received complete revascularization and the ICR group for those subjects who were not completely revascularized. In studies where complete revascularization through CABG and PCI were reported separately, the sum total of completely revascularized patients was used for the complete revascularization group and the remaining patients were added to the ICR group.

Outcomes

The primary outcome used in this systematic study was all-cause mortality. Secondary outcomes were MI and repeat revascularization. Major adverse cardiovascular and cerebral events were also analyzed where present.

Methodological quality

In this meta-analysis, both χ^2 based *Q*-statistic test and I^2 test were considered to assess the heterogeneity across studies, and *P*-value less than or equal to 0.05 was considered significant. I^2 is a description of the variation present across studies that is due to heterogeneity

Table 1 Studies included in meta-analysis

Ref.	Type of search	Method of revascularization	Study design	Year	Definition of CR used	Follow-up (yr)
Bell *et al*[24]	Hand	PCI	Post hoc analysis, non-RCT	1990	Anatomical	2.2
Approach/catherine Mclellan *et al*[25]	Hand	PCI	Post hoc analysis, non-RCT	2005	Anatomical	9
ARTS II/Sarno *et al*[26]	PubMed	CABG/PCI	Post hoc analysis, non-RCT	2010	Anatomical	5
ARTS trial/van den Brand *et al*[14]	PubMed	CABG/PCI	Post hoc analysis, RCT	2002	Anatomical	1
SYNTAX trial/Farooq *et al*[27]	PubMed	CABG/PCI	Post hoc analysis, RCT	2013	Anatomical	4
BARI/Bourassa *et al*[28]	PubMed	CABG/PCI	Post hoc analysis, RCT	1999	Anatomical	5
Bourassa *et al*[29]	Hand	PTCA	Post hoc analysis, non-RCT	1998	Anatomical	9
Head *et al*[30]	PubMed	CABG/PCI	Post hoc analysis, RCT	2012	Anatomical	3
BARI 2D/Schwartz *et al*[31]	PubMed	CABG/PCI	Post hoc analysis, non-RCT	2012	Numerical	5.3
Mohammadi *et al*[32]	Hand	CABG	Post hoc analysis, non-RCT	2012	Anatomical	5.4 ± 3.0

CABG: Coronary artery bypass grafting; PCI: Percutaneous coronary intervention; CR: Complete revascularization; RCT: Randomly controlled trial.

Table 2 Characteristics of patients undergoing complete revascularization

Ref.	Prevalence of CR (%)	Mean age (yr)	Previous MI	No previous MI	Diabetes	No diabetes	Hypertension	No hypertension
Bell *et al*[24]	41.0	60.0	122	234	46	319	148	217
Approach/catherine Mclellan *et al*[25]	66.9	62.1	802	506	244.6	1063.4	725.94	582.06
ARTS II/Sarno *et al*[26]	72.5	61.5	149	688	163	674	440	397
ARTS trial/van den Brand *et al*[14]	77.2	61.0	385	498	143.93	739.07	-	
SYNTAX trial/Farooq *et al*[27]	61.8	65.3	521	1088	429.6	1179.4	759.45	849.55
BARI/Bourassa *et al*[28]	65.4	61.3	612	584	204.52	991.48	578.86	617.14
Bourassa *et al*[29]	17.4	56.6	62	70	15.05	116.95	55.97	76.03
Head *et al*[30]	59.9	64.9	328	713	300	438	702	356
BARI 2D/Schwartz *et al*[31]	37.9	61.21	-		-		-	
Mohammadi *et al*[32]	82.1	82.1	224	167	107.92	283.08	286.21	104.79

CR: Complete revascularization; MI: Myocardial infarction.

instead of chance (I^2 value less than 50% indicates no or little heterogeneity)[7]. Weighted relative risk (RR) and its 95% confidence interval were calculated to evaluate the effect size. A fixed effect model using Mantel-Haenszel method were used to combine values from studies when heterogeneity was absent, otherwise, a random-effects model using the DerSimonian and Laird method was used[8]. Egger's test and inverted funnel plots were utilized to provide a diagnosis of publication bias[9]. Automatic "zero cell" correction was used for studies with no events for a particular outcome. All analyses were performed using Stata version 11.1 software (Stata, College Station, TX, United States). All statistical evaluations were made assuming a two-sided test with a significance level of 0.05, unless stated otherwise.

RESULTS

Study and patient characteristics

The list of the ten studies that met with our inclusion criteria are listed in Table 1. Of the studies included, four were RCTs and six were non-RCTs. All the RCTs reported both CABG and PCI as revascularization strategies. Of the six non-RCTs included, three reported PCI, two reported both CABG and PCI simultaneously, and one reported CABG only. Of the studies comprising our analysis, nine use an anatomical definition of CR and one uses a numerical definition of CR. The current analysis includes 13327 patients of whom, 8053 (60.4%) received complete revascularization (CR) and 5274 (39.6%) received ICR. The mean age of the patients undergoing CR was 63.6 years, 20.5% had diabetes mellitus, 39.8% had suffered from previous MI, 43.5% had hypertension (Table 2). The mean age of the patients undergoing ICR was 65.1 years, 22.4% had diabetes mellitus, 46.1% had previously suffered from MI, and 52.6% had hypertension (Table 3). The mean follow-up time of the patients was 4.9 years.

Mortality

Of the ten studies included, eight reported mortality and were used for this analysis. CR is associated with reduced overall mortality relative to ICR (RR: 0.755, 95%CI: 0.66 to 0.864, P = 0.765, I^2 = 0.0%) (Figure 2). In a subgroup analysis: Mid-term follow-up of < 5 years shows that CR has lower mortality (RR: 0.710, 95%CI: 0.595 to 0.847, P = 0.701, I^2 = 0.0%). Long-term follow-up of > 5 years is associated with reduced mortality (RR: 0.824, 95%CI: 0.669 to 1.016, P = 0.660, I^2 = 0.0%). In the age group of > 60 years, CR is associated with reduced mortality (RR: 0.742, 95%CI: 0.641 to 0.859, P = 0.706, I^2 = 0.0%) (Figure 3).

Table 3 Characteristics of patients undergoing incomplete revascularization

Ref.	Prevalence of CR (%)	Mean age (yr)	Previous MI	No previous MI	Diabetes	No diabetes	Hypertension	No hypertension
Bell *et al*[24]	41.0	60.0	122	234	46	319	148	217
Approach/catherine Mclellan *et al*[25]	66.9	62.1	802	506	244.6	1063.4	725.94	582.06
ARTS II/Sarno *et al*[26]	72.5	61.5	149	688	163	674	440	397
ARTS trial/van den Brand *et al*[14]	77.2	61.0	385	498	143.93	739.07	-	
SYNTAX trial/Farooq *et al*[27]	61.8	65.3	521	1088	429.6	1179.4	759.45	849.55
BARI/Bourassa *et al*[28]	65.4	61.3	612	584	204.52	991.48	578.86	617.14
Bourassa *et al*[29]	17.4	56.6	62	70	15.05	116.95	55.97	76.03
Head *et al*[30]	59.9	64.9	328	713	300	438	702	356
BARI 2D/Schwartz *et al*[31]	37.9	61.21	-		-		-	
Mohammadi *et al*[32]	82.1	82.1	224	167	107.92	283.08	286.21	104.79

CR: Complete revascularization; MI: Myocardial infarction.

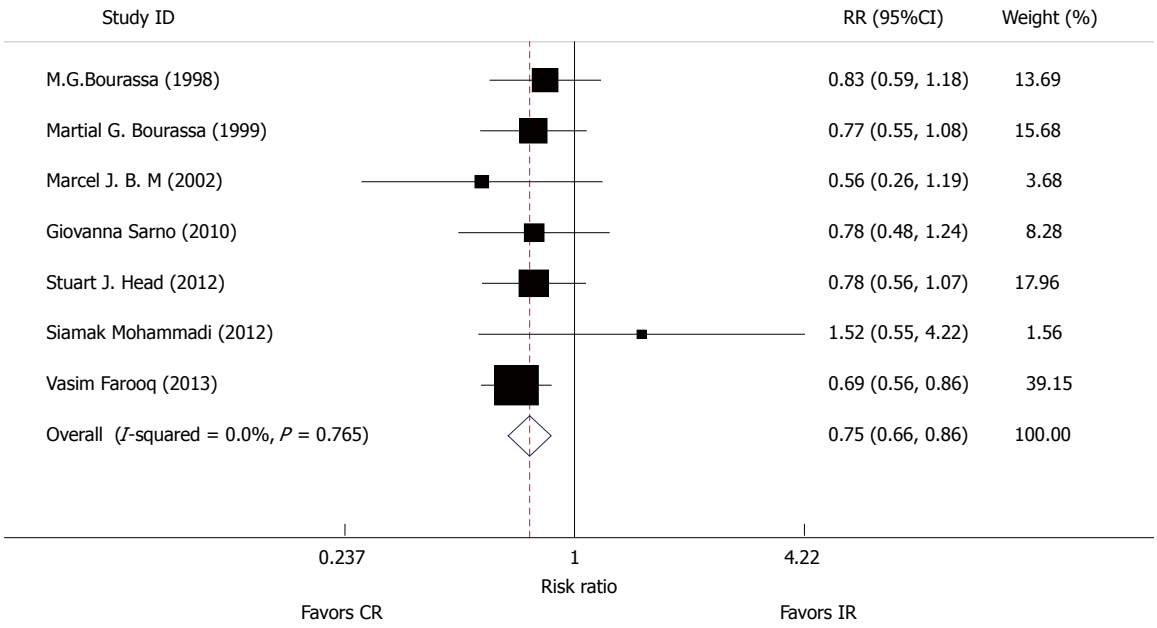

Figure 2 Pooled analysis with risk ratio and 95%CI for the occurrence of total mortality. Boxes are relative risk estimates from each study. The horizontal bars are 95%CI. The size of the box is proportional to the weight of the study in the pooled analysis. CR: Complete revascularization.

MI

Of the ten studies, seven reported MI and were used for this analysis. CR is associated with reduced rates of post-operative MI as compared to ICR (RR: 0.759, 95%CI: 0.615 to 0.937, $P = 0.091$, $I^2 = 45.1\%$) (Figure 4). In a subgroup analysis: mid-term follow-up of < 5 years group, occurrence of MI is less with CR as compared to ICR (RR: 0.608, 95%CI: 0.484 to 0.763, $P = 0.388$, $I^2 = 0.0\%$). Long-term follow-up of > 5 years shows that CR is associated with reduced rates of MI (RR: 0.894, 95%CI: 0.731 to 1.095, $P = 0.419$, $I^2 = 0.0\%$). In the age group of > 60 years, CR is associated with reduced MI (RR: 0.758, 95%CI: 0.589 to 0.974, $P = 0.053$, $I^2 = 54.1\%$).

Repeat coronary revascularization

Of the ten studies, six reported repeat revascularization and were consequently used in this analysis. CR is associated with reduced rates of revascularization (PCI and/or CABG) relative to ICR (RR: 0.691, 95%CI: 0.541 to 0.883, $P = 0.0$, $I^2 = 88.3\%$). In a subgroup analysis: Mid-term follow-up of < 5 years shows that CR is associated with less repeat revascularizations (RR: 0.827, 95%CI: 0.651 to 1.052, $P = 0.323$, $I^2 = 11.6\%$). Long-term follow up of > 5 years shows that CR is associated with less repeat revascularizations (RR: 0.827, 95%CI: 0.651 to 1.052, $P = 0.009$, $I^2 = 78.9\%$). In the age group > 60 years, CR is associated with reduced rates of repeat revascularization (RR: 0.646, 95%CI: 0.484 to 0.863, $P = 0.0$, $I^2 = 89.2\%$).

MACCE

Of the ten studies, five reported MACCE and were used in this analysis. CR is associated with reduced MACCE relative to ICR (RR: 0.731, 95%CI: 0.668 to 0.8, $P = 0.453$, $I^2 = 0.0\%$). In a subgroup analysis of MACCE: Mid-term follow-up of < 5 years shows that CR is associated with lower MACCE rates as compared to ICR

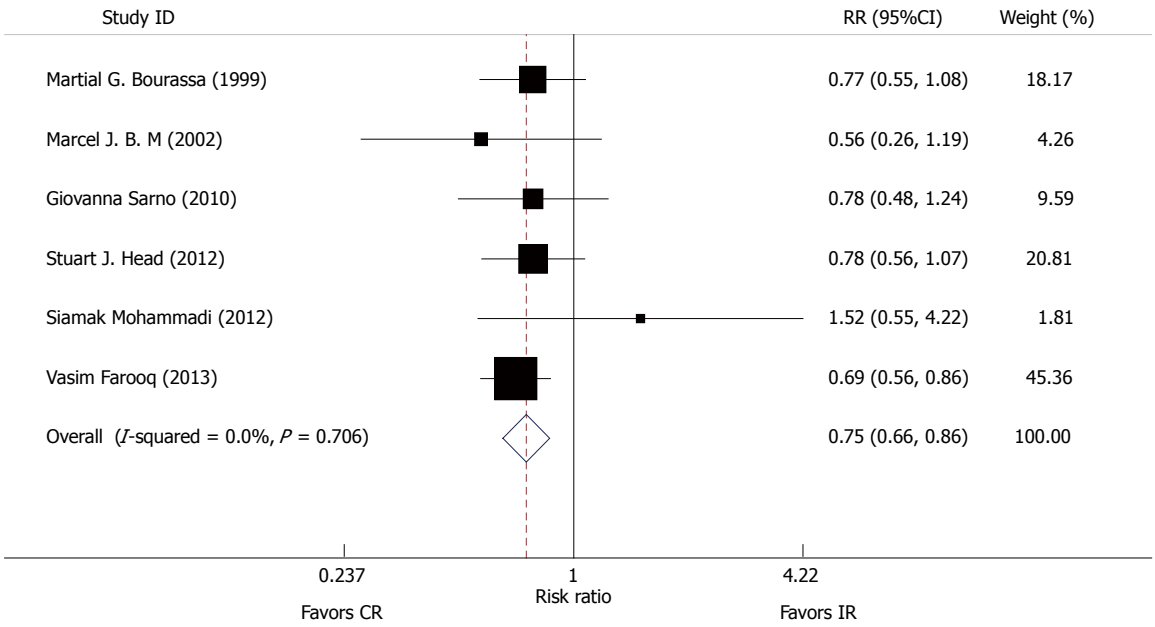

Figure 3 Pooled analysis with risk ratio and 95%CI for the occurrence of mortality in the > 60 age group. Boxes are relative risk estimates from each study. The horizontal bars are 95%CI. The size of the box is proportional to the weight of the study in the pooled analysis. CR: Complete revascularization.

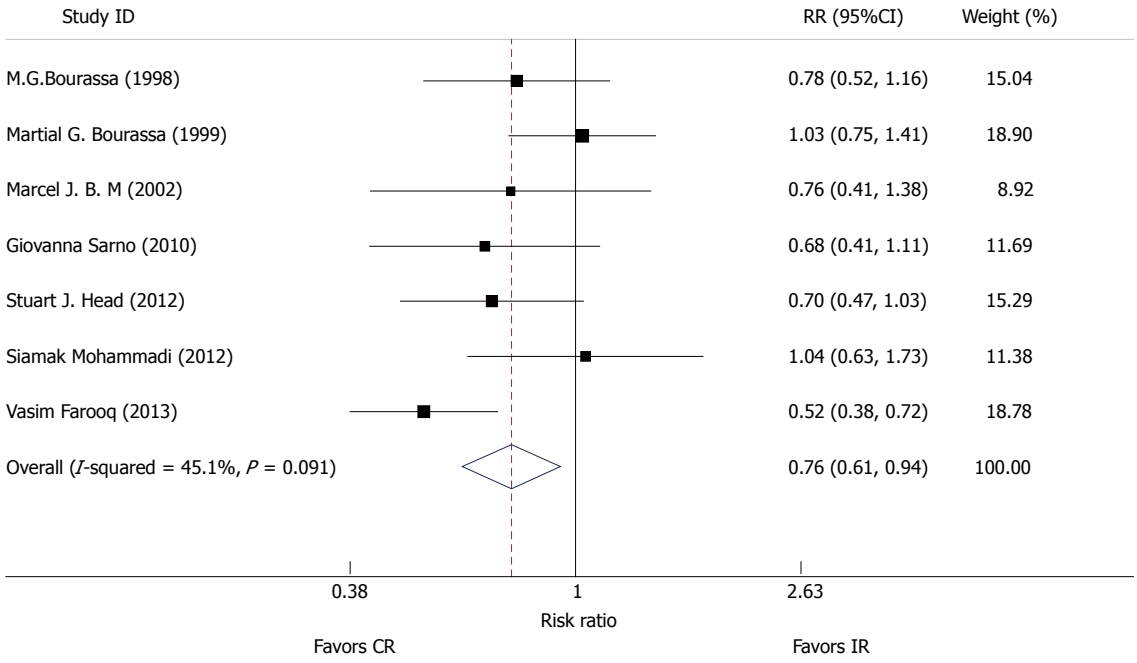

Figure 4 Pooled analysis with risk ratio and 95%CI for occurrence of myocardial infarction. Boxes are relative risk estimates from each study. The horizontal bars are 95%CI. The size of the box is proportional to the weight of the study in the pooled analysis. CR: Complete revascularization.

(RR: 0.717, 95%CI: 0649 to 0.792, P = 0.427, I^2 = 0.0%). Long-term follow-up of > 5 years shows that CR is associated with reduced rates of MACCE (RR: 0.799, CI: 0.644 to 0.990, P = 0.427, I^2 = 0.0%). In the age group of > 60 years, CR is associated with less MACCE (RR: 0.731, 95%CI: 0.668 to 0.8, P = 0.453; I^2 = 0.0%).

DISCUSSION

The results of our study comparing the outcomes of CR *vs* ICR show that CR is associated with a 25% reduction in overall mortality, 24% reduction in MI, 27% reduction in MACCE, and 31% reduction in repeat revascularization procedures. Our findings are quite similar to the paper published by Santiago *et al*[5] where they reported a 30% reduction in long term mortality, a 22% reduction in MI, and a 26% reduction in repeat coronary revascularization procedures. Moreover, the results of our subgroup analysis show that independent of the modality of revascularization, CR is associated

with better mid-term (< 5 years), long-term (> 5 years) outcomes and is also associated with lesser adverse outcomes in the > 60 years old patient population.

Conventionally, there are two distinct approaches to coronary artery revascularization, one of them being CABG and the other being PCI. Both of these revascularization strategies have their set of advantages and disadvantages. The advantages of PCI include use of local anesthesia, minimal post-procedural morbidity, and shorter hospital stay. New advancement in the form of DES has also allowed effective treatment of long diffuse stenosed segments. Despite these numerous advantages, PCI remains restricted with respect to its inability to overcome chronic total occlusions, whereby success rates vary and symptomatic failures eventually require CABG. CABG surgery, on the other hand, despite having the ability to overcome chronic occlusions, and necessitating fewer repeat revascularization procedures, is nevertheless associated with substantial postoperative morbidity, longer periods of hospitalization, and a slower return to normal activities. Multiple diseased vessel segments are challenging, requiring multiple grafts and longer operative times which translate into longer periods of CPB, and are associated with higher morbidity[10]. Among the main adverse outcomes, PCI is associated with higher rates of MI and repeat revascularization while CABG is associated with higher morbidity and risk of stroke[11]. Many variables have to be considered when selecting a patient for any procedure, which might be a cause for dissimilarities between the outcomes from different studies. Although SYNTAX reported a higher incidence of MACCE at 5 years, data concerning the incidence of death, MI and stroke at 5 years was inconsistent between these studies, even in the diabetic subgroup. In SYNTAX there was no significant difference reported at 5 years in any of the individual outcomes of death, MI, or stroke between PCI and CABG in either the diabetic or non-diabetic subgroups[12]. On the other hand, in the FREEDOM trial PCI was associated with higher incidence of death and MI with a lower incidence of stroke when compared to CABG[10]. Past studies have compared post-procedural outcomes of these two revascularization approaches[13-15]. The primary focus of our study is the clinical outcome(s) of complete revascularization as compared to ICR, achieved by any particular method of revascularization, or both methods simultaneously (hybrid procedures), rather than a comparison of CABG *vs* PCI.

Benefits of CR

The association between CR and lower risk for subsequent cardiovascular events has been documented in some studies in which the benefits of complete revascularization are reduction and often elimination of myocardial ischemia (which has been linked to worse prognosis especially when large), improvement in left ventricular function with preserved ejection fraction in heart failure patients, reduction of arrythmias, improved exercise capacity, and better tolerance to future acute myocardial ischemic events[12,16]. More importantly, the mortality benefit of CR is independent of revascularization modality and definition of CR used[17]. In a study by An Den Brand *et al*[14], the authors reported that the frequency with which CR was achieved was greater in CABG treated patients (84.1%) as compared to stented patients, despite the potential for equivalent revascularization. Although no difference in mortality or the combined endpoint of death/stroke/MI were seen, overall MACCE rates were significantly higher in the incompletely revascularized stented group, driven by an increased need for CABG within the first year of follow up.

Over the past decades, CABG has evolved to better peri-operative management, more frequent use of arterial grafting and off pump surgery, and development of minimally invasive direct coronary artery bypass grafting (MIDCAB) and robot-assisted totally endoscopic coronary artery bypass (TECAB) grafting as genuine options. PCIs, especially percutaneous transluminal coronary angioplasty (PTCA), initially developed as a strategy in the treatment of single-vessel disease. Currently, particularly with the advent of DES and new devices to treat chronic total occlusions, it is considered an alternative to CABG in the treatment of multiple vessel disease in certain cases[18,19]. These improvements in technique have increased the feasibility and practicability of complete revascularization. Although CABG and PCI have their own sets of inclusion and exclusion criteria, overlapping in selection criteria exist, where the decision to proceed with a particular technique is generally made by a heart team, consisting of both cardiac surgeons and cardiologists among others. All other factors excluded, we propose that CR/IR should influence a decision to proceed with any specific surgical approach of coronary artery revascularization.

Mid/long-term outcomes

The short-term, mid-term, and long-term outcomes of a strategy of revascularization are as important to the patient as it is to the doctor, and we consider it a pivotal factor in the decision making process. In our study, we sub-divided the follow-up time at the 5-year mark, and obtained the two sub-groups, namely the mid-term follow-up group (< 5 years) and long-term follow-up group (> 5 years). Statistical analysis was separately performed on each of the subgroups. CR was found to be associated with less mortality, post-op MI, reduced MACCE, and repeat revascularization procedures.

> 60 years old

There has been a gradual increase in the average age of patients now referred for CABG. Contemporary cohorts consist of a greater proportion of octogenarians[15,20]. The BARI trial reported no survival disadvantage associated with IR, where non-LAD territories were left ungrafted. Siamak Mohammadi *et al*[32] in their study of octogenarians undergoing CABG reported that short-term and long-term

mortality were not negatively affected by a strategy of ICR during CABG. Due to the greater number of grafted vessels, CR is associated with longer procedural times. This translates into increased duration of general anesthesia, longer cardiopulmonary bypass times, which increase the incidence of negative post-procedural complication and delay discharge from the hospital. Hence, some surgeons have advocated the concept of incomplete "reasonable" revascularization[21-23]. The results of our subgroup analysis show that there is a reduction across all negative outcomes associated with CR in patients who are > 60 years old. Despite the general trend in the elderly population, we propose CR as a precautionary measure against leaving potential myocardial regions and graftable target coronary arteries un-revascularized.

Study limitations

There are several limitations to our meta-analysis. The results are affected by variation in study design, end-point definitions and reporting and possible publication bias. Moreover, our results and analysis are limited to the papers found on the Pubmed database and those added by hand-search.

Our study is concordant with similar studies from the past, whereby CR is associated with lower mortality, reduced post-op MI and MACCE, and lower rates of repeat procedures for revascularization. Furthermore, our study shows that CR is also associated with better mid-term and long-term outcomes, and less adverse outcomes in the > 60 years of age patient population. In our experience, CR acts as a buffer between CABG and PCI, and reduces the adverse outcomes associated with any one particular technique. With this in mind, and as dictated by the patient's condition, the technique with which CR is most likely to be accomplished should be used, and hybrid techniques can be emphasized for complicated cases, thus maximizing the gains from both techniques while minimizing the drawbacks. Given the obvious benefits, CR should be considered as the standard to determine the strategy of revascularization in patients with multi-vessel CAD.

ARTICLE HIGHLIGHTS

Research background

Two strategies are used in the treatment of multivessel coronary artery disease (CAD), namely percutaneous coronary intervention with stenting and coronary artery bypass grafting. Previous studies have proved the importance of complete revascularization. However, the extent to which completeness of revascularization influences the outcomes is still unclear.

Research motivation

Nowadays with new improvements in technology and technique, the feasibility of complete revascularization is less of an issue. Hence, a thorough understanding of how complete revascularization affects post-procedural outcomes is mandatory.

Research objectives

To investigate the influence and outcomes of complete *vs* incomplete myocardial revascularization in patients with multivessel CAD.

Research methods

Database (pubmed) search coupled with hand search was performed for the identification and collection of relevant studies. Filters, inclusion and exclusion criteria were used to ensure quality and homogenecity of studies. Standard tables were used for data extraction. The data was analyzed and subjected to the appropriate tests by a statistician. A systematic review was then performed.

Research results

Ten studies were identified, including 13327 patients of whom, 8053 received complete revascularization and 5274 received ICR. Relative to ICR, CR was associated with lower mortality (RR: 0.755, 95%CI: 0.66 to 0.864, $P = 0.765$, $I^2 = 0.0\%$), lower rates of MI (RR: 0.759, 95%CI: 0.615 to 0.937, $P = 0.091$, $I^2 = 45.1\%$), lower rates of MACCE (RR: 0.731, 95%CI: 0.668 to 0.8, $P = 0.453$, $I^2 = 0.0\%$) and reduced rates of repeat coronary revascularization (RR: 0.691, CI: 0.541 to 0.883, $P = 0.0$, $I^2 = 88.3\%$).

Research conclusions

Completeness of revascularization is not mandatory for the treatment of multivessel CAD. The results of our study show that CR is associated with lower rates of adverse outcomes. The results propose that the extent to which a technique can achieve complete revascularization should be a major deciding factor in the choice of any one particular technique.

Research perspectives

Complete revascularization is an alternative standard to decide the choice of a particular technique of revascularization. With emerging techniques of coronary revascularization, new retrospective cohort studies can be performed. Further research is needed to better understand the benefits of complete revascularization with a particular technique.

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