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Demineralized cortical fibers are associated with a low pseudarthrosis rate in patients undergoing surgery for adult spinal deformity without three-column osteotomy

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A R T I C L E I N F O

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A B S T R A C T

Introduction: Following surgical treatment for adult spinal deformity (ASD) there is an increased risk of revision surgery due to mechanical failure or pseudarthrosis. Demineralized cortical fibers (DCF) were introduced at our institution aiming to reduce the risk of pseudarthrosis after ASD surgery.
Research question: We wanted to investigate the effect of DCF on postoperative pseudarthrosis compared with allogenic bone graft in ASD surgery without three-column osteotomies (3CO).
Materials & Methods: All patients undergoing ASD surgery between January 1, 2010 to June 31, 2020 were included in this interventional study with historical controls. Patients with current or previous 3CO were excluded. Before February 1, 2017, patients undergoing surgery received auto- and allogenic bone graft (non-DCF group) whilst patients after received DCF in addition to autologous bone graft (DCF group). Patients were followed for at least two years. The primary outcome was radiographic or CT-verified postoperative pseudarthrosis requiring revision surgery.
Results: We included 50 patients in the DCF group and 85 patients in the non-DCF group for final analysis. Pseudarthrosis requiring revision surgery at two-year follow-up occurred in seven (14%) patients in the DCF group compared with 28 (33%) patients in the non-DCF group ($p = 0.016$). The difference was statistically significant, corresponding to a relative risk of 0.43 (95%CI: 0.21–0.94) in favor of the DCF group.
Conclusion: We assessed the use of DCF in patients undergoing ASD surgery without 3CO. Our results suggest that the use of DCF was associated with a considerable decreased risk of postoperative pseudarthrosis requiring revision surgery.

1. Introduction

Pseudarthrosis represents a major cause of revision surgery following surgical treatment of adult spinal deformity (ASD) with incidences reported between 6 and 41% (How et al., 2019; Klineberg et al., 2016; Kim et al., 2006a, 2006b; Dickson et al., 2014; Bari et al., 2021; Smith et al., 2016; Pitter et al., 2019; Diebo et al., 2019). Common risk factors of pseudarthrosis include thoracolumbar kyphosis of >20°, age above 55 years, positive sagittal vertical axis (SVA) ≥5 cm, smoking, fusion to S1 as compared to L5, and more than 12 instrumented levels (Kim et al., 2006a; O'Shaughnessy et al., 2012). Regardless, restoring sagittal balance is essential. Surgical intervention is considered favorable when non-operative management in ASD patients fails (Youssef et al., 2013; Passias et al., 2018; Teles et al., 2017). With the aging population and concomitant expectations of an active lifestyle, the number of ASD surgeries will increase and this could be paralleled by an increase in revision surgery (Safaee et al., 2020; Steinberger et al., 2020). To address this issue, demineralized cortical fibers (DCF) were introduced in 2017 at our institution in all surgical procedures for ASD. Demineralized cortical fibers consist entirely of active demineralized bone matrix (DBM) and therefore do not need a biocompatible viscous carrier. In a recent study of patients undergoing ASD surgery with three-column osteotomy (3CO), the rate of postoperative pseudarthrosis was significantly reduced in patients receiving DCF combined with autologous- and allogenic bone graft compared with autologous- and allogenic bone graft alone (Bari et al., 2021). When 3CO is required for the treatment of ASD the degree of global or local sagittal deformity is often greater than in patients without the need for 3CO (Iyer et al., 2018). Dickinson et al. reported that

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61% of their pseudarthrosis cases occurred at the site of the 3CO and Hallager et al. found that performance of 3CO was associated with a significantly increased hazard of mechanical failure (Dickson et al., 2014; Hallager et al., 2017). These findings suggest that surgeries including 3COs lead to increased pseudarthrosis rates. Therefore, the aim of the study was to assess if the use of DCF in ASD patients without 3CO is associated with decreased pseudarthrosis rates reducing the risk of revision surgery. To the best of our knowledge, no study has previously assessed this matter.

2. Materials & Methods

To determine pseudarthrosis rates in patients undergoing ASD surgery with DCF, we conducted an interventional study with historical controls performed at a single quaternary spine institute. This study was approved by the National Health and Medical Authority and The National Data Protection Agency (30 Nov. 2018 R-21054762; 21 Oct. 2021 P-2021-777).

Adult spinal deformity surgery was defined as all adult patients undergoing surgery for a sagittal deformity with instrumented fusion of $\geq$5 vertebral levels.

2.1. Subjects

All patients undergoing ASD surgery between January 1, 2010, to June 31, 2020 were included in this study. The included patients had a minimum of two-year follow-up. Patients were excluded if the surgical procedure involved a 3CO or if they had previously undergone a 3CO procedure. The intervention group (DCF) underwent surgery after February 1, 2017 and the control group (non-DCF) underwent surgery before February 1, 2017. Both groups underwent the same standard protocol for treatment with the same radiographic examinations preoperatively, immediately postoperatively and at 3 months, 1 year and 2 years postoperatively. Patient demographics including history of previous spine surgery, comorbidities, current surgical procedure, and length of stay (LOS) were collected using electronic medical records. Adverse events (AEs) were prospectively collected during index admission using The Spine AdVerse Event Severity (SAVES) system (Karstensen et al., 2016; Bari et al., 2020a). Patients with postoperative wound infection requiring revision surgery were excluded for final analysis due to the removal of bone graft.

2.2. Pseudarthrosis

Pseudarthrosis was defined as radiographic or CT-verified implant failure (rod breakage, set-screw dislodgement, screw breakage, loosening or pullout) requiring revision surgery (Fig. 1).

2.3. Bone graft

Demineralized cortical fibers were introduced to our institution February 1, 2017. Patients undergoing ASD surgery after February 1, 2017 received DCF in combination with autograft (DCF group), whilst patients undergoing surgery before the cutoff date received allogenic bone graft (femoral head) in combination with autograft (non-DCF group). The inclusion criterion was bone graft placed at L4-S1. The DCF bone graft used in the present study is commercially produced and obtained in sterile, factory-sealed packages. The allogenic bone graft (femoral head) from our local bone bank is sterile, deep-frozen and non-cleaned.

2.4. Surgical procedure

Computer-assisted surgical planning were per standard protocol assessed on all patients using the online imaging system KEOPS (SMAIO, Lyon, France) (Maillot et al., 2015). Preoperative radiographic parameters were analyzed to accurately plan the intended surgical correction. Our institution holds two senior surgeons with more than 25 years of experience each in ASD surgery. A team of at least one senior surgeon and an associate specialist surgeon performed surgery. Patients underwent surgery with posterior pedicle screw instrumentation with Chrome Cobalt rods (2-rod system). Both treatment groups received autologous bone graft harvested during the release, for instance facetectomy, decompression, etc. In all patients, complete facetectomies were done on the instrumented levels followed by decortication along the transverse processes. There have been no major changes in the preparation of the bone bed at our institution in the inclusion period. In the DCF group, 30 mL of DCF was mixed with 24 mL of autologous bone marrow aspirate. In the non-DCF group, patients received one batch allogenic bone graft (femoral head) from the bone bank connected to our hospital. All bone graft material was placed posterolateral in the lumbar region of the spine. Supplementary allogenic bone graft was added where needed proximal of L4. Three-column osteotomy procedures were not indicated in any of the included patients and this decision was taken prior to inclusion in this study.

2.5. Statistics and outcome

All statistical analysis were made using the language and environment of R, version 4.2.0 (R Development Core Team, Vienna, Austria,

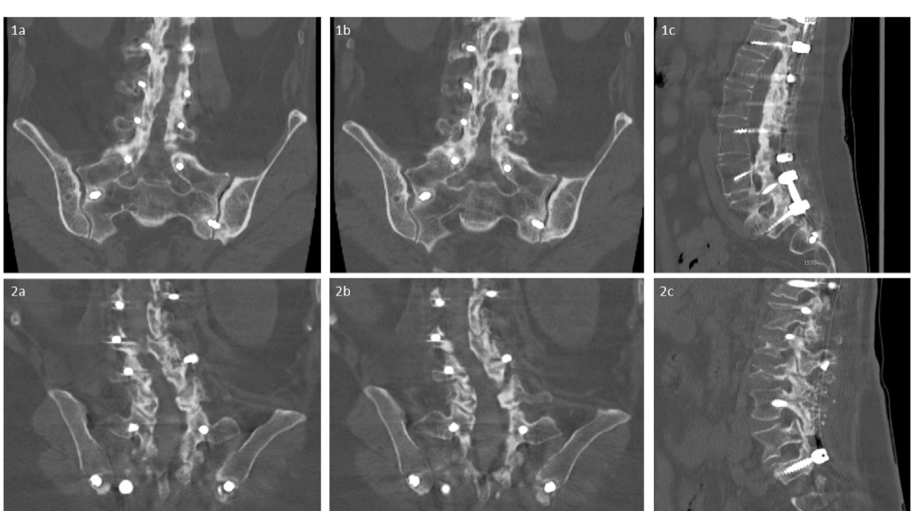

Fig. 1. Two-year postoperative CT-scan of a 54-year-old woman treated with instrumented fusion of Th3–S2 with supplementary autograft and DCF in the lumbar region (1a-1c). The CT-scan shows excellent posterior fusion on two consecutive antero-posterior images (2 mm slice thickness) (1a,1b) and on the sagittal projection (1c).
Fourteen months postoperative CT-scan of a 44-year-old woman treated with instrumented fusion of Th4–S2 with supplementary auto- and allograft in the lumbar region (2a-2c). During a forward bend, the patient experienced a snap followed by immediate pain and radiographs revealed a right-sided rod breakage at L4/L5. Two consecutive antero-posterior images (2a,2b) and sagittal image (2c) revealed pseudarthrosis with non-union and visible facet joints. The patient was revised shortly after.
DCF, demineralized cortical fibers.

2020). Distribution of data was evaluated with histograms and results were reported as means (±SD), medians [IQR] or proportions (%). Student's *t*-test and Wilcoxon's rank-sum test were used to compare Gaussian and non-Gaussian distributed data, respectively. Categorical variables were analyzed and compared using Pearson's X^2 test or Fisher's exact test (for less than 10 observations in individual cells). Moreover, we used Kruskal Wallis test for non-Gaussian distributed data when comparing proportions between three groups or more. The primary outcome was radiographic or CT verified postoperative pseudarthrosis requiring revision surgery assessed using 2-year crude rates. Pseudarthrosis rates were additionally analyzed using a competing risk survival model and illustrated as cumulative incidences. Gray's test was used determine significant difference of cause-specific cumulative incidence between groups. Lastly, uni- and multivariate logistic regression analysis were performed to compare the two groups and results were reported as odds ratios (OR) with 95% confidence interval (CI). P values of <0.05 were interpreted as statistically significant.

3. Results

3.1. Subjects

In the interventional DCF group, we included 50 patients undergoing ASD surgery between February 1, 2017 and June 31, 2020. In addition, 85 patients in the non-DCF group underwent ASD surgery between January 1, 2010 and February 1, 2017 (Table 1). The DCF group had more frequently undergone previous spine surgery and index surgery included more instrumented levels in this group. We found no statistical difference amongst ASD aetiologies between the two groups (Table 2). The DCF group had a significantly greater increase in sacral slope (SS) and global lordosis (GL) compared with the non-DCF group after surgery (Table 3). Pelvic incidence minus lumbar lordosis (PI-LL) was significantly lower postoperatively in the DCF group (Table 3). Major complications were recorded in 16% of patients in the DCF group and 20% in the non-DCF group (p = 0.44). The median pack/year amongst smokers were similar across treatment groups (DCF: 24 [IQR: 12-40] years; non-DCF group: 20 [IQR: 13-39] years, p = 0.859).

3.2. Pseudarthrosis and DCF

At 2-years follow-up, pseudarthrosis requiring revision surgery occurred in seven (14%) patients in the DCF group. This was significantly less than in the non-DCF group, where pseudarthrosis occurred in 28 (33%) patients (p = 0.016). This corresponds to a risk ratio of 0.43 (95% CI: 0.21–0.94) in favor of the DCF group. To highlight the cumulative incidence rates of pseudarthrosis, we used a competing risk model (Fig. 2). Gray's test revealed no significant difference between competing events in the two groups (p = 0.127). Multivariate logistic regression analysis on pseudarthrosis requiring revision surgery showed a significantly decreased odds ratio (OR) of 0.23 using DCF bone graft (Table 4). We found no statistical difference in pseudarthrosis risk stratified by aetiology.

Table 1
Patient demographics stratified in groups of DCF, non-DCF and total.

	DCF (n = 50)	Non-DCF (n = 85)	Total (n = 135)	P-value
Age (years)	63.4 (10.8)	60.8 (12.0)	61.8 (11.6)	0.220
Sex (female)	40 (80%)	63 (74%)	103 (76%)	0.440
Previous surgery	37 (74%)	48 (57%)	85 (63%)	0.042*
Previous instrumentation	28 (56%)	24 (28%)	52 (39%)	0.018*
Previous instrumentation ≥4 vertebrae	21 (42%)	12 (14%)	33 (24%)	<0.001*
No. of previous surgeries	2.3 (1.9)	1.5 (0.8)	1.8 (1.4)	0.011*
Instrumented vertebrae	16 [10-17]	11 [9-15]	12 [9-16]	<0.001*
CCI score	3 [1.25–3]	2 [1-3]	2 [1-3]	0.026*
LOS	9 [2-14]; ; ;	10 [10-17]; ; ;	9 [2–14]	0.483
Smoker (current or previous)	27 (54%)	49 (58%)	76 (56%)	1.000
BMI	26.3 (7.1)	26.2 (5.0)	26.2 (5.8)	1.000

Data are mean (±SD), median [IQR] or counts (%) *Indicates p-value <0.05 **DCF:** Demineralized cortical fibers, **CCI:** Carlson Comorbidity Index, **LOS:** Length of stay, **BMI:** Body mass index.

Table 2
ASD aetiology stratified in groups of DCF, non-DCF and total.

	DCF (n = 50)	Non-DCF (n = 85)	Total (n = 135)	p-value
Idiopathic Scoliosis	18 (36%)	30 (36%)	48 (36%)	1.000
De-novo Scoliosis	3 (6%)	13 (15%)	16 (12%)	0.181
Hyperkyphosis	10 (20%)	13 (15%)	23 (17%)	0.642
Iatrogenic sagittal deformity	14 (28%)	24 (28%)	38 (28%)	1.000
Secondary (traumatic, infectious, neoplasm)	5 (10%)	5 (6%)	10 (7%)	0.588

Data are counts (%) **ASD:** Adult spinal deformity, **DCF:** Demineralized cortical fibers.

Table 3
Radiographic parameters stratified in groups of DCF, non-DCF and total.

	DCF (n = 50)	Non-DCF (n = 85)	Total (n = 135)	P-value
Pelvic incidence (°)				
Preoperative	50.7 (11.7)	54.2 (16.3)	52.9 (14.8)	0.187
Postoperative	52.7 (14.1)	53.4 (14.8)	53.2 (14.5)	0.762
Pelvic tilt (°)				
Preoperative	22.8 (9.6)	24.7 (11.2)	24.0 (10.6)	0.326
Postoperative	18.6 (9.8)	22.2 (12.2)	20.9 (11.5)	0.073
Surgical correction	−4.2 (9.7)	−2.5 (10.2)	−3.1 (10.0)	0.328
Sacral slope (°)				
Preoperative	27.9 (11.6)	29.5 (14.5)	28.9 (13.5)	0.497
Postoperative	34.1 (11.2)	31.1 (13.5)	32.2 (12.7)	0.186
Surgical correction	6.4 (10.7)	1.6 (10.9)	3.4 (11.0)	0.016*
Global lordosis (°)				
Preoperative	43.1 (15.5)	47.0 (19.0)	45.6 (17.9)	0.219
Postoperative	54.0 (13.1)	49.1 (16.4)	50.9 (15.4)	0.076
Surgical correction	10.6 (13.1)	2.0 (13.4)	5.1 (13.9)	<0.001*
Global kyphosis (°)				
Preoperative	56.6 (22.5)	52.8 (19.1)	54.2 (20.5)	0.293
Postoperative	59.6 (15.7)	53.8 (16.6)	55.9 (16.4)	0.049*
Surgical correction	2.2 (14.4)	1.0 (13.5)	1.5 (13.8)	0.064
SVA (mm)				
Preoperative	89.5 (62.1)	78.1 (73.4)	82.3 (69.4)	0.360
Postoperative	44.5 (44.9)	49.6 (44.2)	47.8 (44.3)	0.524
Surgical correction	−44.6 (59.5)	−28.5 (60.1)	−34.3 (60.1)	0.139
PI-LL (°)				
Preoperative	14.1 (16.2)	14.1 (17.9)	14.1 (17.2)	0.984
Postoperative	−1.2 (12.0)	6.6 (16.1)	3.8 (15.2)	0.004*
Number of lordotic vertebrae				
Preoperative	4.8 (2.0)	4.4 (1.8)	4.5 (1.9)	0.194
Postoperative	5.5 (1.2)	4.9 (1.2)	5.1 (1.3)	0.010*
Surgical correction	0.7 (2.1)	0.5 (1.8)	0.6 (1.9)	0.654

Data are mean (±SD) or counts (%)*Indicates p-value <0.05 **DCF:** Demineralized cortical fibers, **SVA:** Sagittal vertical axis, **PI-LL:** Pelvic incidence minus lumbar lordosis.

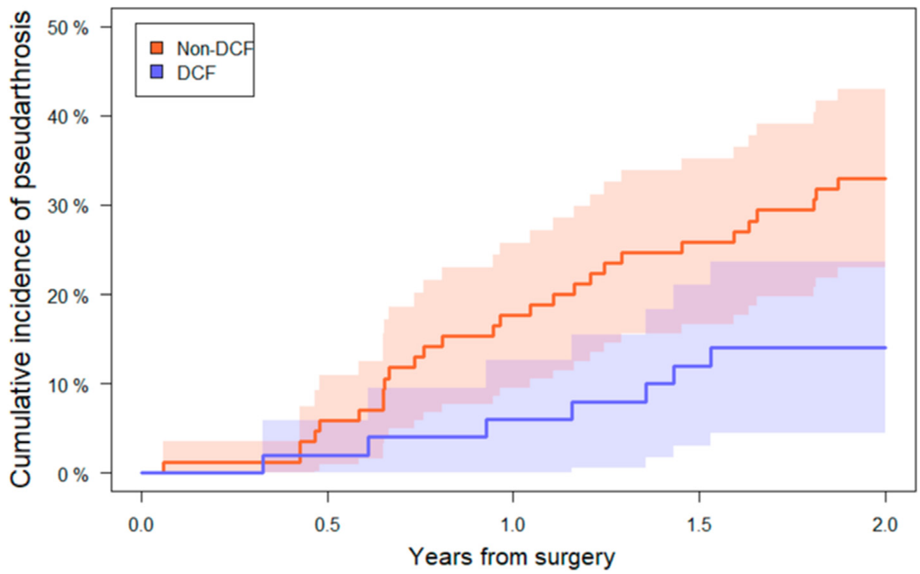

Fig. 2. Cumulative incidence rate plot of radiographic or CT-verified pseudarthrosis requiring revision surgery between the two groups revealed a decreased risk in the DCF group compared to the control, corresponding to a significantly decreased relative risk.DCF, demineralized cortical fibers.

Table 4
Predictors of pseudarthrosis using logistic regression analysis.

	Univariable OR [95% CI]	p	Multivariable OR [95% CI]	p
DCF	0.25 [0.11;0.55]	<0.001*	0.22 [0.09:0.52]	<0.001*
Age (yrs)	0.96 [0.94;1.00]	0.023*	0.97 [0.91:1.03]	0.252
No. of instrumented levels	1.00 [0.91;1.09]	0.933	1.02 [0.92:1.15]	0.671
CCI	0.76 [0.59;0.98]	0.034*	1.01 [0.63:1.61]	0.963
Sex	0.68 [0.30;1.54]	0.352	0.54 [0.20:1.42]	0.212
Smoker (current or previous)	1.54 [0.77;3.11]	0.222	1.31 [0.58:2.98]	0.518
BMI	0.98 [0.92;1.04]	0.499	0.97 [0.90:1.05]	0.451

Data are odds ratio with 95% confidence interval*Indicates p-value <0.05 **DCF:** Demineralized cortical fibers, **CCI:** Carlson Comorbidity Index, **BMI:** Body mass index, **OR:** Odds ratio, **CI:** Confidence interval.

4. Discussion

The findings in this study suggests that adding DCF during ASD surgery can markedly reduce the risk of postoperative pseudarthrosis requiring revision surgery.

4.1. Subjects

Rates of pseudarthrosis requiring revision surgery was significantly lower in the DCF group compared with the non-DCF group. The rate of revision surgery in the present study is similar to that of other ASD studies (Hallager et al., 2017; Bari et al., 2020b). Patients in the DCF group had more often undergone previous instrumented spine surgery, had more comorbidities and had more fused levels during index surgery. Smith et al. found a significantly higher proportion of rod fractures among patients with a history of previous spine surgery (Smith et al., 2014). Pitter et al. found a positive correlation between comorbidity burden and the risk of revision surgery (Pitter et al., 2019). Kim et al. suggested that posterior fusion instrumentation of more than 12 vertebrae was associated with increased pseudarthrosis rates (Kim et al., 2006a). O'Shaughnessy et al. found increased pseudarthrosis rates in patients with long fusion (T3-Sacrum) compared with short fusion (T10-Sacrum) (O'Shaughnessy et al., 2012). We found no significant difference in smoking or pack/year amongst smokers between the two groups. Despite these findings, the DCF group still had significantly lower pseudarthrosis rates in our study.

4.2. Radiographic parameters

Previous studies have shown that greater malalignment in baseline spinopelvic parameters in ASD patients undergoing surgery equals a higher frequency of rod fracture (Smith et al., 2014). We found no significant differences between groups in preoperative sagittal parameters. This could be explained by the selection of patients for ASD surgery in the current cohort – most having a severe deformity – and to the notion that a biological outcome (pseudarthrosis) should be less affected by a radiographic parameter (sagittal balance). We did record significant differences between the groups in certain postoperative sagittal parameters. The surgical correction of GL increased more in the DCF-group. The DCF-group did have a smaller GL preoperatively, although not significant, without any postoperative difference between the groups. Both postoperative global kyphosis and PI-LL was significantly different, most likely as a consequence of the non-significantly greater GL in the DCF-group. Both groups had a mean PI-LL below the threshold of mismatch (PI-LL<10°) (Schwab et al., 2013). We found no difference between groups on SS, preoperatively and postoperatively, however, did record a difference in surgical correction of SS. We are convinced that these differences are of minor impact on the rate of pseudarthrosis.

4.3. Pseudarthrosis

Due to the lack of previous studies on DCF in ASD surgery, comparing the current results to previous findings is difficult. To our knowledge, only our institution has previously published clinical data on the use of DCF in ASD surgery (Bari et al., 2021). This was supported by the literature review by Shepard et al. who reported no publications on the clinical use of DCF (Shepard et al., 2021). Demineralized cortical fibers and DBM have similar osteoinductive properties but an animal study performed on rabbit models by Martin et al. suggested that DCF does have greater osteoconductive properties compared with DBM particulate (Martin et al., 1999). These findings were later confirmed in another in-vivo study performed on rat models (Russell et al., 2020). In the study by Bari et al., the pseudarthrosis rate of 15% in the DCF group and 41% in the control allograft group was similar to the rates in the current study (Bari et al., 2021). Previous reports of the effect of DCF in ASD surgery are indeed sparse and similarly other types of DBM use within ASD surgery are limited. To the best of our knowledge, no previous study has reported the rate of pseudarthrosis following ASD surgery including DBM. As a surrogate measurement, we found that several studies suggest non-inferior fusion rates when comparing DBM as an adjunct to local autologous autograft with iliac crest bone graft (ICBG), allograft and Bone Morphogenetic Protein-2 (BMP-2) following lumbar fusion surgery (Buser et al., 2018; Fu et al., 2016; Han et al., 2020; Eleswarapu et al., 2021).

4.4. Bone graft

Since Moe et al. introduced ICBG in 1958, supplemental bone graft has been considered an important contributor to achieving spinal fusion (John, 1958). Demineralized cortical fibers are one of several available bone grafts used in spinal surgery. Focusing on other types of bone grafts, Scheer et al. developed a computer-based preoperative predictive model for pseudarthrosis in 336 ASD patients in a retrospective, multicenter study (Scheer et al., 2018). Autograft, allograft and BMP-2 were the posterior graft types included in the study (Scheer et al., 2018). The authors concluded that the second most important predictor of pseudarthrosis was posterior BMP use. This was further highlighted by Paul et al. who reported a pseudarthrosis rate of 5% at 4-year follow-up in ASD patients when using BMP-2 (Kadam et al., 2016). The authors defined ASD surgery as patients aged 21 years or older with idiopathic scoliosis (Kadam et al., 2016). This contrasts with our ASD definition and the subsequent patient population as idiopathic scoliosis merely represented 36% of the included patient population (Table 2).

Despite these differences in rates of pseudarthrosis between different types of bone grafts, previous studies have also suggested otherwise. How et al. found similar outcomes between available graft material in ASD surgery (How et al., 2019). The prospective multicenter study by Smith et al. reports no association between different bone graft types and the occurrence of rod fracture (Smith et al., 2016). The included bone graft types were allograft, ICBG, locally harvested autograft, DBM and BMP-2 (Smith et al., 2016). Notwithstanding the lack of agreement, we believe our findings show a strong association between the use of DCF and low pseudarthrosis rates in patients undergoing ASD surgery.

4.5. Three-column osteotomy procedures

The study conducted by Bari et al. only included patients undergoing ASD surgery with 3CO (Bari et al., 2021). Inarguably, 3CO procedures are associated with higher rates of pseudarthrosis (Smith et al., 2016; Scheer et al., 2018). One could argue that the percentage of cases with pseudarthrosis in our study should be considerably less frequent compared with that of Bari et al. (2021). However, all patients in our study underwent ASD surgery with sacral fusion. In Bari et al.'s study, only 75% of the DCF group had instrumentation to the sacrum (Bari et al., 2021). It is commonly known that long posterior instrumented fusion to the sacrum increases the risk of pseudarthrosis compared with terminating the fusion at L5 (How et al., 2019; Kim et al., 2006a, 2006b; Scheer et al., 2018; Jia et al., 2020). However, the benefits of fusion to the sacrum, as opposed to L5, generally outweigh the risks in most ASD cases; e.g. restoring sagittal balance, no subsequent advanced L5-S1 disc degeneration, and no distal junctional failure etc. (Jia et al., 2020; Taneichi et al., 2020; Kuhns et al., 2007; Pateder et al., 2006). Smith et al. reported a significantly higher rate of rod fracture in ASD surgeries with pedicle subtraction osteotomy (PSO) procedures compared with non-PSO procedures (22.0% vs. 4.7%) (Smith et al., 2016). The multivariate analysis suggested that PSO procedures were associated with a significantly increased odds ratio of rod fracture (OR 5.76. 95% CI 2.01–15.8) (Smith et al., 2016). Undoubtedly, ASD patients in need of 3CO procedures do belong to a more severe patient group where greater surgical correction is often needed with consequent increased risks of postoperative complications (Daubs et al., 2007; Boachie-Adjei et al., 2015).

5. Limitations

We do recognize several limitations of this study. The primary endpoint was pseudarthrosis requiring revision surgery. Arguably, a more precise outcome could have been assessing posterolateral fusion in all patients using CT assessment. We do argue that radiographic classification of fusion or non-fusion is not as clinically relevant as revision surgery. This is why we chose to use pseudarthrosis requiring revision surgery as our primary endpoint. This difference hinders direct comparison of pseudarthrosis rates between bone grafts. Most studies assessing bone grafts in ASD surgery evaluated fusion on either CT or radiographs and defined fusion according to the Lenke Classification or the Modified Glassman Scale (Lenke et al., 1992; Carreon et al., 2007). Pseudarthrosis on a radiographic scan is not necessarily symptomatic and does therefore not always necessitate further intervention as discussed previously. Vice versa, successful fusion does not always lead to satisfactory clinical outcomes (Chang et al., 2021; Fischgrund et al., 1997; Herkowitz and Kurz, 1991). The outcome for this study was therefore defined as an outcome with definite clinical impact, i.e. pseudarthrosis requiring revision surgery. Several confounding factors in the current study need to be considered. One possible explanation for the difference between the two groups could be the obvious discrepancy in inclusion periods. Patients in the DCF group were included in the period of February 1, 2017 to mid-2020 in contrast to patients in the non-DCF group, who were included from 2010 to February 1, 2017. Possible changes in diagnostics, surgical planning and treatment might influence the results – though we believe this cannot explain the entire difference in pseudarthrosis rates. The difference in surgical correction between the two groups could influence the rate of pseudarthrosis. We do argue that this influence is minor due to similar postoperative radiographic parameters. Comparing interventional cohorts with historical controls, the matter of learning curve might influence the results. We believe this to have minimal impact on our findings. Our institution's two senior surgeons have performed ASD surgeries for more than 2 decades. Other potential confounders are smoking and body mass index but we found no significant differences between groups on these parameters. We hypothesize the reason for smoking not being a significant risk factor in our study is because of small cohort numbers.

Overall, our findings are of great importance to both patients and clinicians. A reduction of revision surgeries at two-year follow-up by more than 50% is significant. This benefits both the patients with fewer revision surgeries and thereby lightens the financial and clinical burden on the health care system. For further studies, we propose assessing pseudarthrosis rates at 5- and even 10-year follow-up because of the known continuous elevation of pseudarthrosis risks after two-year follow-up (Pichelmann et al., 2010). Additionally, we believe that the strong association between DCF and decreased pseudarthrosis rate is sufficient to suggest future randomized controlled trials to determine causal correlation.

6. Conclusion

We found a clinically relevant and statistically significant reduced risk of pseudarthrosis requiring revision surgery in ASD patients undergoing surgery without 3CO procedures with DCF combined with autograft compared with allograft adjunct to autograft. The findings suggest that DCF is a valid and good choice when deciding on a specific bone graft to use in ASD patients. Further randomized studies are necessary to validate the findings.

Ethical approval

This study was approved by the National Health and Medical authority and The National Data Protection Agency.

Funding details

No external funding was received.

Informed consent

This study includes no experimental investigation.

Availability of data and material

The datasets generated during and/or analyzed during the current study are not publicly available due to national data protection law.

Code availability

Code can be made available upon reasonable request.

Author contribution

Martin Heegaard: Substantial contributions to the conception or design of the work, Substantial contributions to the acquisition, analysis and interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published.

Tanvir Johanning Bari: Substantial contributions to the conception or design of the work, Substantial contributions to the analysis and interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published.

Benny Dahl: Substantial contributions to the conception or design of the work, Revising the work critically for important intellectual content, Final approval of the version to be published.

Lars Valentin Hansen: Substantial contributions to the conception or design of the work, Revising the work critically for important intellectual content, Final approval of the version to be published.

Martin Gehrchen: Substantial contributions to the conception or design of the work, Revising the work critically for important intellectual content, Final approval of the version to be published.

Declaration of competing interest

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