Pre-existing vertebral fracture is a risk factor for postoperative proximal junctional fracture after adult spinal deformity surgery: A propensity score-matched analysis

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**A B S T R A C T**

Background: Corrective surgery for adult spinal deformity has recently been increasingly performed because of aging populations and advances in minimally invasive surgery. Low bone mineral density is a major contributor to proximal junctional kyphosis after spinal long fusion. Assessment for low bone mineral density ideally involves both dual energy X-ray absorptiometry and identification of pre-existing vertebral fractures, the latter, requiring only standard equipment, being performed more frequently. We therefore aimed to examine the impact of pre-existing vertebral fractures on the incidence of type 2 proximal junctional kyphosis, including proximal junctional fracture and failure, after corrective surgery for adult spinal deformity.

Methods: We performed a retrospective, single institution study of 106 women aged over 50 years who had undergone corrective long spinal fusion for severely symptomatic spinal deformity from 2014 to 2017. We allocated them to three groups (with and without pre-existing vertebral fractures and with severe [Grades 2–3 according to Genant et al.’s classification] pre-existing vertebral fractures) and used propensity score matching to minimize bias. The primary outcome was postoperative proximal junctional fracture and the secondary outcome proximal junctional kyphosis/failure.

Results: The primary and secondary endpoints were achieved significantly more often in the 28 patients with than in the 78 without preexisting vertebral fractures (total 41). The former group was also significantly older and had greater pelvic tilt and fewer fused segments than those without vertebral fractures. After propensity score matching, the incidences of the endpoints did not differ with pre-existing vertebral fracture status; however, patients with severe vertebral fractures more frequently had proximal junctional fractures postoperatively. Postoperative improvements in health-related quality of life scores did not differ with pre-existing vertebral fracture status.

Conclusions: Severe pre-existing vertebral fractures are a risk factor for proximal junctional fracture after correction of adult spinal deformity.

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1. Introduction

Corrective surgeries have been increasingly performed on adults with spinal deformity (ASD) in the last 15 years because of aging populations and introduction of innovative minimally invasive surgical techniques [1,2]. The health-related quality of life (HRQOL) of patients with ASD reportedly improves significantly with surgery, despite the high frequency of associated complications, especially in older individuals [3]. Proximal junctional kyphosis (PJK) is a widely recognized complication of spinal long fusion, its incidence reportedly being as high as 20%–40% [1]. Yagi et al. have reported a modified classification of PJK into three types. Type 2 with bone failure, also called proximal junctional fracture (PJF), often requires additional surgery for serious complications such as neurological impairment [4], such complications generally being defined as proximal junctional failure (PJF) [1,5].

PJK, including PJFr and/or PJF, has multifactorial causes, surgery-related factors including excessive sagittal correction, large
postoperative pelvic incidence minus lumbar lordosis mismatch, and long spinal fusion including the sacrum and pelvis [5,6]. Patient-related factors are age >55 years, high body mass index (BMI), preoperative spinal malalignment, and low bone-mineral density (BMD) [7–9].

Dual-energy X-ray absorptiometry (DXA) is the gold standard for evaluating BMD. Both identification of pre-existing vertebral fractures (VF) and findings on DXA are important aspects of assessment, various osteoporosis guidelines indicating that these are high priority risk factors for bone fragility [10,11]. Previous studies have reported the prevalence of osteoporosis and incidence of VF [12,13], and the relationship between pre-existing and secondary VF in healthy adults [14]; however, none have examined the impact of pre-existing VF on postoperative PJFr and PJK/PJF in patients undergoing ASD surgery. In this study, the primary outcome was the postoperative complication of PJFr, the secondary outcome being PJK/PJF. We investigated the incidence of PJFr and PJK/PJF in patients grouped according to pre-existing VF status.

In comparisons in an entire cohort, mismatching of patient characteristics between groups can bias results. To avoid this, we adopted propensity score matching (PSM), a balancing technique for adjusting covariates and estimating causal effects in observational studies in which random assignment is difficult and various confounding factors are possible [15,16]. The purpose of this study was to use PSM to determine whether pre-existing VF is a risk factor for complications of ASD surgery.

2. Materials and methods

2.1. Study design and patient cohort

This is a retrospective study of data in a single institution. The cohort comprised patients with ASD with lumbar or thoracolumbar deformity and severe back pain, stooped posture, and gait disturbance attributable to their spinal imbalance who had undergone corrective surgery between 2014 and 2017. Inclusion criteria were patients with ASD aged ≥50 years at the time of surgery, abnormal radiographic variables (Cobb angle ≥20°, or sagittal vertical axis [SVA] ≥ 4 cm, or pelvic tilt [PT] ≥ 30°) undergoing corrective long spinal fusion of six or more spinal segments, and postoperative follow-up for ≥2 years. We excluded patients with spinal deformity associated with Parkinson disease, Parkinson syndrome, neuromuscular scoliosis, other syndromic scoliosis disorders, and deformity caused by high energy trauma or tumor.

In accordance with the selection criteria, we included 106 patients (all women) of mean age 67.3 ± 8.7 years (range: 50–83 years) at surgery and with a mean duration of follow-up of 36 months (range: 24–59 months). The causes were as follows: adult idiopathic scoliosis (29 patients), de novo spinal deformity (kyphoscoliosis; 51), spinal kyphosis (18), and iatrogenic spinal deformity (8).

2.2. Main outcome measures

This study was approved by our institution’s review board. We reviewed patients’ charts and radiographs. The main outcome measures were age, BMI, DXA of femoral neck, history of VF, number and level(s) of VF at the time of surgery, preoperative antosteoporosis medications (teriparatide and bisphosphonate [BP]), levels of upper instrumented vertebra (UIV) and lower instrumented vertebra (LIV), and number of fusion segments. We reviewed the incidence of the postoperative complications of PJK/PJF and PJFr, using the definition of PJK proposed by Glattes et al. [17]. We defined PJF as requiring revision surgery for PJK because of severe pain and/or neurological deficit [5]. We defined PJFr as Type 2 PJK/PJF in Yagi et al.’s classification [4].

Anteroposterior and lateral full-length standing whole spine radiographs were obtained preoperatively, 1, 2, 3, 6, 9, and 12 months postoperatively, then every 6 months thereafter. We measured SVA, PT, and pelvic incidence minus lumbar lordosis (PI–LL) in the sagittal plane and classified these variables in accordance with the Scoliosis Research Society–Schwab ASD classification [18], and change in lumbar lordosis (LL). We identified pre-existing VF by examining preoperative whole spine radiographs and classified them as Grade 0–3 based on the semi-quantitative (SQ) grading proposed by Genant et al. [19]. Patients with acute symptomatic VF and old VF with pseudoarthrosis were excluded. We allocated patients with Grade 0 to a ‘non_VF group’, those with Grade 1, 2 or 3 to a ‘VF group’, and those with Grades 2 or 3 to a ‘severe VF group’. Using these radiographic outcomes, we determined the incidence of postoperative complications at the latest follow-up. We also recorded patients’ femoral neck BMD T-scores using DXA. Each patient completed two self-assessed HRQOL measures: the Oswestry disability index and Scoliosis Research Society (SRS)-22 questionnaire, preoperatively and at latest follow-up.

2.3. Comparison methods and statistical analysis

We compared patient characteristics and baseline data, preoperative sagittal radiographic variables and surgical data (UIV, LIV, number of fusion segments, change in LL and postoperative PI–LL), and postoperative incidence of PJFr and PJK/PJF between the non_VF, VF, and severe VF groups in the entire and propensity-matched cohorts. Additionally, we compared HRQOL scores immediately preoperatively and at latest follow-up between these groups in propensity-matched cohorts.

PSM analysis based on a linear model was used to adjust for differences in baseline patient data between the three study groups. Covariate analysis included age, BMI, cause, preoperative SRS–Schwab ASD categorization (curve type, SVA, PT, PI–LL), change in LL, postoperative PI–LL, UIV level, LIV level, and number of fused segments (Table 1). Fig. 1 shows the flow chart for patient selection.

Normal distribution of the data was demonstrated with the Shapiro–Wilk test. Student’s t-test was used to compare normally distributed data between the study groups and the Mann–Whitney test to compare non-normally distributed data. Fisher’s exact test was used to adjust categorical variables (numbers and percentages) between the groups. Odds ratios were adjusted after PSM calculations using Fisher’s exact test. P < 0.05 was considered to denote statistical significance. All statistical analyses were performed using SPSS 26.0 software (SPSS, IBM, Armonk, NY, USA).

3. Results

3.1. Patient characteristics, radiographic findings, surgical data and incidence PJK/PJFr/PJF in the entire cohort

The 106 study patients were allocated to a non_VF group of 78 patients and a VF group of 28 patients that included 16 patients with severe VF (SQ Grade ≥2). A total of 41 preexisting VFs were identified, including multiple fractures in one patient; 14 VFs (34.1%) were located in T8–T12, 15 VFs (36.6%) in L1–L2, and 12 VFs (29.3%) in L3–L5. All patients underwent pre- and postoperative whole spine radiographs; however, only 56 patients (52.8%) underwent DXA of the femoral neck. Eighteen patients (17.0%) had
received teriparatide and 15 (14.2%) had received BP as anti-osteoporosis treatment preoperatively.

As to the three sagittal modifiers of the SRS-Schwab ASD classification, SVA was 91.1 ± 59.4 mm, PT 33.4 ± 9.9°, and PI–LL 40.4 ± 20.2°. No patients had SRS-Schwab T curves, four had D curves, 81 L curves, and 21 N curves. The number of fused segments was 9.2 ± 2.2, the change in LL was 22.6 ± 5.0° and in postoperative PI–LL 61.5 ± 15.7°. The UV level was upper thoracic in 14 patients (13.2%) and lower thoracic in 92 (86.8%). The LL level was located at L5 in 15 patients (19.8%) and in the sacrum or pelvis in 85 (80.2%; Table 1).

The incidences of PJK/PF/PF/PJ between the group with two or fewer segments and the group with three or more segments [PJK; 46.2%; 60.0%, PJF; 38.4%; 60.0%, PJF; 23.1%; 20.0%, respectively].

3.2. Comparison between non-VF, VF and severe VF groups in the entire cohort

Patients in the VF and severe VF groups were older than in the non-VF group (non-VF vs. VF, severe VF; age 65.6 ± 9.0 vs. 72.0 ± 5.7 years, p < 0.01, 72.9 ± 5.5 years, p < 0.01). Fewer patients had received teriparatide in the non-VF than the VF and severe VF groups (teriparatide; 11.5% vs. 32.1%, p < 0.01, 43.8%, p < 0.01), whereas a similar proportion of patients had received BP in these three groups. There were statistically significant differences in cause between the non-VF and VF or severe VF groups. There were no patients with pre-existing VF or severe VF among those with adult idiopathic scoliosis (adult idiopathic scoliosis: de novo spinal deformity: spinal kyphosis: iatrogenic spinal deformity: 37.2%: 11.5% vs. 32.1%, p < 0.01, 43.8%, p < 0.01), whereas a similar proportion of patients had received BP in these three groups. There were statistically significant differences in cause between the non-VF and VF or severe VF groups. There were no patients with pre-existing VF or severe VF among those with adult idiopathic scoliosis (adult idiopathic scoliosis: de novo spinal deformity: spinal kyphosis: iatrogenic spinal deformity: 37.2%: 11.5% vs. 32.1%, p < 0.01, 43.8%, p < 0.01).

PT was greater in the VF and severe VF than non-VF group (PT; 32.0 ± 9.8 vs. 37.3 ± 9.4°, p < 0.01, 41.2 ± 9.0°, p < 0.01). PI–LL was...
higher in the severe VF than non-VF group (PL−LL; 38.9 ± 20.4 vs. 48.4 ± 21.1, p < 0.05). There were fewer fused segments in both the VF and severe VF groups than in the non-VF group (levels fused: 9.4 ± 2.4 vs. 8.6 ± 0.9, p < 0.01, 8.7 ± 0.9, p < 0.05). More patients had Type L curves (Schwab-SRS ASD classification) in the non-VF than in the VF group (Type L; 82.1% vs. 60.7%, p < 0.01). More patients had upper thoracic UIV levels in the non-VF than VF group (upper thoracic; 17.9% vs. 0%, p < 0.05). The other assessed variables, including change in LL and postoperative PI−LL, UIV, LIV and number of fusion segments were similar between the groups. T-scores and BMD tended to be lower in the VF and severe VF groups than in the non-VF group; however, this difference was not significant (Table 1).

The incidences of PJK/PJFr/PJF were significantly higher in the severe VF than non-VF group (PJK; 29.5% vs. 56.3%, p < 0.05; PJK; 15.4% vs. 56.3%, p < 0.001; Table 2).

3.3. Comparison between study groups in the propensity-matched cohort

Propensity score-matching was performed to minimize the effects of differences in patient’s characteristics between the groups. DXA of the femoral neck was not included in the covariates in PSM because data were available for only 53% of patients. Ultimately 44 patients were enrolled in the PSM analysis between non-VF and VF patients (22 in each group) and 26 in the PSM analysis between non-VF and severe VF patients (13 in each group; Fig. 1).

Assessed patient characteristics, including age, BMI, cause, preoperative antosteoporosis medications, preoperative radiographic variables, change in LL, postoperative PI−LL, UIV, LIV and number of fusion segments were similar in the propensity-matched non-VF and VF groups (Table 3). There were no statistically significant differences in the incidences of PJK, PJFr or PJF in these two groups after PSM (Table 4.)

Assessed patient characteristics, including age, BMI, cause, preoperative antosteoporosis medications, preoperative radiographic variables, change in LL, postoperative PI−LL, UIV, LIV and number of fusion segments were also similar in the propensity-matched non-VF and severe VF groups (Table 5). The incidence of PJFr was significantly higher in the severe VF than non-VF group (adjusted odds ratio 8.8; PJFr 15.4% vs. 61.5%, P < 0.05, 95% CI: 1.3–57.4) after PSM. There were no statistically significant differences in the incidences of PJK and PJF between these two groups after PSM (Table 4).

HRQOL scores preoperatively and at the latest follow-up after PSM are shown in Table 6, which shows that T, ODI,
and SRS-22 scores were significantly improved at final follow-up compared with preoperative values in all groups. There were no differences between the non-VF and VF or severe VF group in many domains both preoperatively and at final follow-up; however, the score for the satisfaction domain of SRS-22 at the final follow-up was higher in the non-VF than the VF or severe VF group (4.0 ± 0.8 vs. 3.3 ± 0.7, p < 0.05, 4.2 ± 0.5 vs. 3.4 ± 0.7, p < 0.05).
4. Discussion

In this study, the incidences of PJK/PJFr/PJF were higher in both the pre-existing VF and severe VF groups than in the non-VF group in the entire cohort. However, after performing PSM, the incidences of PJK/PJFr/PJF were similar in the pre-existing VF and non-VF groups. In contrast, the incidence of PJF was higher in the pre-existing severe VF (62%) than non-VF group (15%; odds ratio 8.8).

According to previous studies, older age (>55 years), low BMD, high BMI, sagittal malalignment at baseline, large correction, and pelvic fusion are independent risk factors for PJF, including PJK and/or PJF [1,4–9]. In the present study’s entire cohort, the VF group (including severe VF) were older and had larger PT and shorter fusion segments than the non-VF group; these characteristics were adjusted as covariates during PSM. To the best of our knowledge, this is the first study to demonstrate the impact of pre-existing severe VF on PJF after corrective surgery in patients with ASD.

No clear definition of PJF has been established; it is generally defined as proximal junctional angle ≥10°–20°. In this study, we defined PJF as ≥10° in accordance with Glattes et al. [17] and as used in many reports. Bridwell et al. suggested PJK ≥20° to capture more serious conditions after ASD surgery [20]; however, they found that PJK ≥20° had no effect on revision surgery and SRS outcome scores. Proximal junctional angle is commonly measured when evaluating adjacent segmental problems around the UIV; however, assessing the presence of a fracture around the UIV is simple and reliable. Using PJFr rather than PJF as the primary outcome is another novel aspect of this study.

Intergroup comparison after PSM adjustment showed that only the incidence of PJFr was significantly higher in the severe VF than non-VF group; PJK and PJF did not differ between these groups. PJFr reportedly comprises 56% of PJK [4], which is consistent with the 66% (23 patients) rate of PJFr among all PJK patients (38) in this study. We expected a significant difference in PJFr, this being strongly associated with osteoporosis and secondary VF. Using PJF as the surrogate endpoint of possible complications is contentious because it is defined as PJK that requires revision surgery and therefore depends on the indications for surgery and patient preferences [1,4–9]. For example, some patients with PJK or PJFr...
with severe deformity or pain do not undergo surgery for various reasons, including comorbidities. This may explain the discrepant results of this study in terms of PJK/PJFr/PJF.

Yagi et al. who incorporated PSM in their study, reported that low BMD (T-score < −1.5) is a risk factor for PJF [21]. DXA is the gold standard for evaluating bone strength in patients with osteoporosis [22]; however, it is less frequently performed than spinal X-rays. In standard for evaluating bone strength in patients with osteoporosis low BMD (T-score < −2.5) is assessed. DXA is the preferred method for evaluating BMD as a surrogate marker for osteoporosis and indicator of bone density. DXA requires additional equipment and radiation exposure. The validity of using pre-existing VF rather than BMD as a surrogate marker for osteoporosis and indicator of bone density is uncertain; however, one group has reported that VF severity according to radiograph-based SQ grading correlates with BMD in the femoral neck and whole body [23].

Whether SQ Grade 1 indicates non-clinically relevant VF is controversial [24–26]. However, there is consensus that severe VF (Grade 2 or 3) is associated with low BMD [10,12,23], which is consistent with the high incidence of PJFr in the severe VF group in this study. It is widely recognized that the relative risk of secondary VF can be quadrupled by previous VF [14]. Because PJFr is essentially a form of secondary VF, it is inevitably present in patients with osteoporosis-related pre-existing VF undergoing ASD surgery. We believe that an increase in stress on upper adjacent segments secondary to long spinal fusion and alignment correction resulted in the higher incidence of PJFr in the severe VF group in our study. Various preventive measures against PJF, including PJFr and PJF, have been reported [27]. In terms of surgical technique, PJF can be prevented by using transverse process hooks at UIV rather than using pedicle screws alone [28]. Additionally, preserving the interspinous ligament and facet joint around the UIV may help to maintain posterior support strength. However, this maneuver is not sufficient [29] and no reported procedure completely prevents postoperative PJK. There is no question that osteoporosis treatment aimed at increasing and maintaining BMD is important. Two studies have evaluated osteoporosis interventions and the incidence of PJF in patients with ASD undergoing corrective surgery. In a case–control study with T-scores < −1.1, Yagi et al. reported that the group receiving prophylactic teriparatide (BMD = 0.771 ± 0.219 g/cm²) had a significantly lower incidence of PJF and the incidence of PJFr (PJF/PJFr Type 2) was 4.6% (2/43 cases) [30]. Seki et al. also reported that patients receiving teriparatide (BMD = 0.652 ± 0.128 g/cm²) had a lower incidence of revision surgery, including PJF, than patients receiving BP; the incidence of PJF was 9.1% (3/33 cases) [31]. Of the patients with pre-existing VF in the present study, 32% had received teriparatide preoperatively. It may be possible to reduce the PF incidence by giving more patients prophylactic teriparatide; however, this is unlikely to completely prevent PJF. Introduction of a prophylactic medication such as abaloparatide may better prevent new VF [32]. Surgeons should inform patients with ASD and severe VF and their families that they may be at increased risk of postoperative PJF and discuss pharmacological interventions for osteoporosis. Primary ASD surgery is not urgent; it is therefore ideally performed after evaluation of, and adequate treatment for, osteoporosis in patients at risk of bone fragility. Reduction in incidence of new VF by administration of teriparatide can be expected only after receiving it for at least 12 months [33]. Therefore, if possible, patients with severe osteoporosis should wait for at least one year before corrective spine surgery.

Finally, this study had several limitations. First, despite our use of PSM, there may still be case selection bias because this was a small retrospective study, not a randomized controlled trial. Given that the entire cohort comprised women, our findings cannot validly be applied to all patients undergoing ASD surgery. The second limitation is the small proportion of patients who underwent DXA (53%), which made it difficult to determine the relationship between PJFr and low BMD. Including both radiograph-based SQ grading and BMD by DXA would enable construction of a highly accurate multivariate analysis model for patients with ASD.

Third, patients’ comorbidities and information about anti-osteoporosis medications were not well documented. Patients

### Table 6

Preoperative and latest follow-up health related quality of life in propensity-matched patient cohorts.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (106)</th>
<th>Propensity-matched non-VF vs. VF</th>
<th>Propensity-matched non-VF vs. severe VF</th>
<th>Propensity-matched non-VF vs. severe VF</th>
</tr>
</thead>
<tbody>
<tr>
<td>ODI</td>
<td>Preoperative</td>
<td>40.0 ± 19.0</td>
<td>38.8 ± 13.6</td>
<td>51.3 ± 20.5</td>
</tr>
<tr>
<td></td>
<td>Latest follow-up</td>
<td>22.1 ± 13.6</td>
<td>21.8 ± 14.8</td>
<td>26.3 ± 9.9</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.000***</td>
<td>0.01*</td>
<td>0.003**</td>
</tr>
<tr>
<td>SRS-22 Function</td>
<td>Preoperative</td>
<td>3.1 ± 0.9</td>
<td>2.9 ± 0.6</td>
<td>2.6 ± 0.8</td>
</tr>
<tr>
<td></td>
<td>Latest follow-up</td>
<td>3.8 ± 0.7</td>
<td>3.6 ± 0.8</td>
<td>3.5 ± 0.3</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.000***</td>
<td>0.03*</td>
<td>0.004**</td>
</tr>
<tr>
<td>Pain</td>
<td>Preoperative</td>
<td>3.2 ± 0.8</td>
<td>3.3 ± 0.8</td>
<td>2.8 ± 0.9</td>
</tr>
<tr>
<td></td>
<td>Latest follow-up</td>
<td>4.1 ± 0.7</td>
<td>4.1 ± 0.8</td>
<td>3.9 ± 0.8</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.000***</td>
<td>0.000***</td>
<td>0.004**</td>
</tr>
<tr>
<td>Self-image</td>
<td>Preoperative</td>
<td>1.9 ± 0.5</td>
<td>1.9 ± 0.4</td>
<td>1.9 ± 0.6</td>
</tr>
<tr>
<td></td>
<td>Latest follow-up</td>
<td>3.9 ± 0.7</td>
<td>3.9 ± 0.7</td>
<td>3.8 ± 0.6</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.000***</td>
<td>0.000***</td>
<td>0.000***</td>
</tr>
<tr>
<td>Mental</td>
<td>Preoperative</td>
<td>2.8 ± 0.9</td>
<td>2.5 ± 0.7</td>
<td>2.7 ± 0.9</td>
</tr>
<tr>
<td></td>
<td>Latest follow-up</td>
<td>3.8 ± 0.7</td>
<td>3.7 ± 0.9</td>
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</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.000***</td>
<td>0.000***</td>
<td>0.002**</td>
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<tr>
<td>Satisfaction</td>
<td>Preoperative</td>
<td>3.7 ± 0.7</td>
<td>4.0 ± 0.8</td>
<td>3.3 ± 0.7</td>
</tr>
</tbody>
</table>

ODI, Oswestry Disability Index; PJFr, proximal junctional fracture; SRS, Scoliosis Research Society; VF, vertebral fracture.
P < 0.05, **P < 0.01, ***P < 0.001.
* Student’s t-test or.
† Mann–Whitney U test was used to compare propensity-matched non-VF group and propensity-matched VF group or propensity-matched severe VF group.
* Wilcoxon’s signed-rank test was used to compare preoperative and latest follow-up data.

#### References

with severe hip arterial cirrhosis, hemorrhoid disorders, collagen disease, and rheumatoid arthritis were not included in this cohort, whereas those with diabetes mellitus, mild heart disease, and respiratory disease were. These confounding factors may affect postoperative VF as a risk factor for PJFr (adjusted odds ratio 10.0). Surgeons should prioritize prevention of postoperative PJFr after corrective surgery in ASD patients with severe VF.

Declaration of competing interest

None.

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References


