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ORIGINAL ARTICLE

Prospective study of the effect of pedicle screw placement on development of the immature vertebra in an in vivo porcine model

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Abstract
Introduction There is increasing awareness of the need for pedicle screw constructs in the treatment of spinal deformities in very young children. However, the long-term effects of pedicle screws on the immature spine are still unclear. We used a porcine model to analyze the morphological changes of the spinal canal and vertebral body in response to the placement of pedicle screws.
Methods 13 newborn pigs were operated on. Each pig received a single pedicle screw at the L2 level. After a tenfold increase in body weight (7 months later), the symmetry of the spinal canal and vertebral body was measured on CT scans of the investigational (L2) and control (L3) levels in terms of the angulations of the instrumented and non-instrumented halves of the vertebral body and spinal canal.
Results After 7 months, the normalised vertebral body angle had reduced on the non-screw side and increased on the screw side, indicating asymmetry in vertebral body growth in the axial plane. The difference was significant ($p = 0.009$). However, there was no significant difference between the screw and non-screw sides for the spinal canal angles at the L2 level at either the intraoperative or 7-month follow-up assessment (each $p > 0.05$).
Conclusions Pedicle screws in the immature porcine spine have a significant effect on the development of the vertebral body. However, in the present study, no corresponding alteration of the morphology of the spinal canal was observed. Our results provide further support for the existing arguments in favour of pedicle screws when weighing up the many factors to be considered in creating a treatment plan for early onset scoliosis.

Keywords Pedicle screw · Porcine model · Vertebra development · Early onset spinal deformity (EOS, EOSD)

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Introduction

Spinal deformity in the growing spine can have a major effect on skeletal growth and the development of various organs. The first 5 years of life are especially important in terms of development of the lungs, alveoli, chest wall, and unaffected regions of the spine. Early onset spinal deformity (EOSD, also known as Early Onset Scoliosis) often necessitates spinal surgical intervention to correct the deformity in order to prevent irreversible damage to the aforementioned structures.

For several reasons, pedicle screw-rod constructs have become increasingly popular in the treatment of spinal deformities in adolescents and adults. They have excellent biomechanical properties and are suitable for the transfer and subsequent maintenance of large correction forces in all planes [1]. There is an increasing tendency in spinal deformity surgery to use posterior only approaches with pedicle screw systems. These constructs are also suitable for the treatment of EOSD for the same biomechanical reasons as in adults. Although pedicle screw systems adapted in size for paediatric use have recently become available, there is a certain reluctance to use them in very young patients for a number of reasons. First, pedicle screws crossing the neurocentral cartilage might cause dysfunction in growth, which in turn could theoretically contribute to further progression of the deformity. Second, especially in cases with complex anatomical aberrations, inserting pedicle screws safely can be quite challenging. Third and probably most important, it is assumed that the insertion of pedicle screws in the growing spine will result in spinal canal stenosis and subsequent neurological compromise.

Only few studies have used animal models to investigate the effect of pedicle screws on spinal canal morphology in the immature spine [2–4], and these have arrived at contradictory conclusions regarding the subsequent growth of the spinal canal.

The purpose of this prospective study was to examine the effects of pedicle screws on spinal canal and vertebral body growth in immature pigs.

Materials and methods

Pigs are often used for experimental purposes in spinal research and implant testing, mainly because of the anatomical similarities to humans [2, 3, 5, 6]. In addition, the accelerated life cycle of pigs compared to humans renders them especially suitable for experiments concerning growth and development.

In order to make our porcine model as accurate and reliable as possible, we applied the same freehand screw insertion technique that we use in our daily surgical practice in humans. To get acquainted with the porcine anatomy, we first performed a pilot study with 10 domestic pigs that were being sacrificed for reasons unrelated to our study. CT scans between Th9–11 and L2–L4 were performed to assess the anatomy of these regions. Based on these findings the second lumbar vertebra (L2) was chosen as the level to use for instrumentation. Subsequently, pedicle screws were inserted into L2 on both sides using a free-hand technique. The screw position was verified intraoperatively with fluoroscopy. Following that, thin slice CT scans were carried out to assess the exact screw position. After gaining sufficient experience in pedicle screw placement in pigs, we commenced the actual study on the effects of pedicle screws on the developing spine [7]. This animal study was conducted in accordance with the ethical policy of the Faculty of Veterinary Medicine of the University.

Study design

We used 13 domestic white pigs (9 females and 4 males) from 2 mothers. They were 38–45 days old and weighed 8.3 kg (range 6.0–11.5 kg) at the time of surgery. The animals were killed 7 months later, at the age of 8.5 months, after they had reached a tenfold increase in their body weight (97.2 kg; range 94.5–103.0 kg). Using a calculation that considered data for skeletal maturity based on closure of the epiphysis of long bones, and growth charts describing growth potential and immaturity [8], the model was designed to correspond to children growing from the age of 6 months to 4 years. The time span between the surgery and the final analysis was chosen to include the most active growth period of the neurocentral junction.

To reduce the stress on the pigs and to minimize the approach-related growth disturbance and complication rate, we chose to perform as minimal a surgery as possible, inserting just a single pedicle screw in each pig. Furthermore, instrumentation of just one vertebra was not expected to result in spinal deformity, allowing us to avoid any potential secondary effect of deformity on vertebral development. For the reasons described above, the L2 vertebra was selected for instrumentation. We assumed that insertion of a screw on one side only would affect the growth of only that side. If any growth disturbance due to screw insertion should occur, this would hence be expected to result in asymmetry as the contralateral side continued to grow unaltered. The side of instrumentation (right or left) was randomly assigned. Screws were placed on the right side in six animals and on the left in seven animals.

General anaesthesia

Just before the surgery, Calypsovet inj. (ketamin) 8 mg/kg and Rompun inj. (xylasin) 1 mg/kg was delivered intramuscularly. The animals were then intubated and maintained on isoflurane gas with oxygen. During the surgery saline (Salsol) 10 ml/kg was administered. Antibiotic prophylaxis using 0.4 ml/5kg Shotapen (benzathine penicillin 100 mg/procaine penicillin 100 mg/streptomycin 0.164 iu/100 ml) was applied in the immediately postoperative period. The antiobiotics were administered again, 3 days after surgery. The animals were administered Metacam inj. (meloxicam) 0.2 mg/kg/day subcutaneously for 3 days as postoperative analgesia.

Surgical technique

The animals were placed in a prone position. After shaving, and sterile preparation and draping of the surgical field, the appropriate side of the lumbar spine at the L2 level was exposed, taking care not to injure the periosteal layer. Avoidance of subperiosteal preparation was expected to reduce the risk of growth disturbance unrelated to the pedicle screws per se. The cranio-caudal extension of the approach was kept to a minimum, with the L3 level being left intact. The exposure was extended sufficiently laterally to expose the base of the transverse process, to facilitate anatomical orientation, but the rest of the transverse process was left intact, again to avoid any approach-related growth disturbance. After determining the entry point, a 1.5 mm diameter hole was drilled. The integrity of the bony canal through the pedicle was tested with a ball-tip instrument of 1 mm diameter. Subsequently, according to the length of the drilled canal, 18–22-mm-long cancellous full thread self-tapping ACE titanium screws (DePuy) with an outer diameter of 4.0 mm and with a core diameter of 2.8 mm were inserted. The length of each surgical procedure averaged 30 min. There were no instances of pedicle wall perforation (which would otherwise have resulted in exclusion of the case).

Following surgery, the animals were kept under general anaesthesia, and a CT scan was performed to obtain axial cuts at the L2 (instrumented level) and at the L3 level (uninstrumented reference level). A final CT scan was performed in a similar fashion 7 months after the surgery.

Radiological analysis

Measurements were performed on the CT scans to quantify the symmetry of the spinal canal and the vertebral body. For these purposes, angles were measured describing each side of each vertebra (L2 and L3) as follows. Angles to measure vertebral body asymmetry: a line was firstly drawn connecting the intersection of the neurocentral cartilage with the spinal canal and the most anterior aspect of the vertebral body in the immature pigs (or the anterior crista of the vertebral body in the adult animal) on each side (Fig. 1). The angle between this line and the horizontal plane was then measured on each side and defined as the vertebral body angle–non-screw side (VBa-ns) or vertebral body angle–screw side (VBa-s).

Angles to determine spinal canal symmetry: a line was drawn connecting the most posterior point of the spinal canal and the junction of the spinal canal and neurocentral junction (Fig. 2). The angle between this line and the horizontal plane was defined as the spinal canal angle–non-screw side (SCa-ns) or spinal canal angle–screw side (SCa-s).

An independent radiologist performed all CT measurements twice in each CT study.

Intrarater reliability calculations revealed no significant differences between repeated measurements ($p > 0.05$) and intraclass correlation coefficients of 0.92–0.99, indicating excellent reliability.

Statistical analyses

Descriptive data are presented as means and standard deviations (SD).

The duplicate measurements for all dimensions were first averaged to give a representative value for the given vertebral level and side (screw or non-screw).

The values for L2 (the intervention level) were then normalised to (i.e. expressed as a proportion of) the corresponding value at the level below (L3; control level), to account for any possible alterations in the positioning of the animal during imaging at the different time-points, and to account for normal changes in the angles over time due to growth. Non-parametric Wilcoxon Signed Rank tests were used to examine the significance of the difference between sides (screw/non-screw) for: (1) the normalised L2 angles at the intraoperative assessment; (2) the normalised

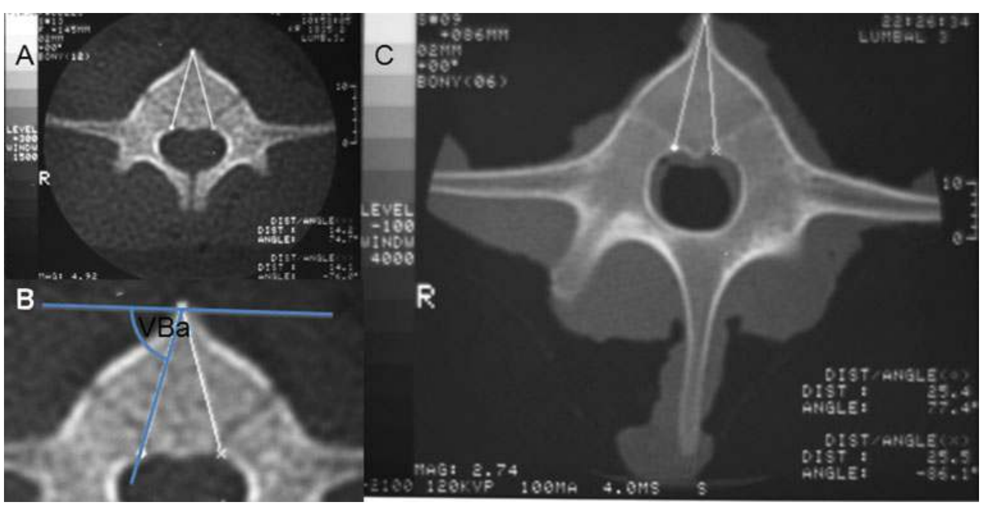

Fig. 1 This figure shows axial CT cuts at the third lumbar vertebra level. The *lines* indicate how the vertebral body angle (*VBa*) on both sides was determined. *VBa* is defined as an angle of a line between the intersection of the neurocentral cartilage with the spinal canal and the most anterior aspect of the vertebral body and the coronal plane. **a** Immediately postoperative CT image. **b** Same as A, but zoomed in. **c** CT scans 7 months postoperatively

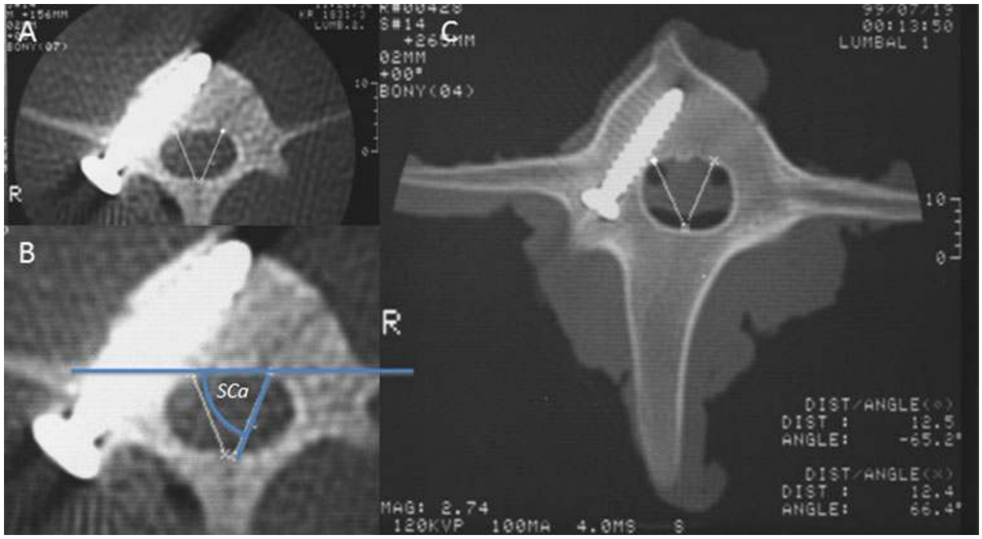

Fig. 2 Similarly to Fig. 3, this figure shows axial CT cuts at the second lumbar vertebra level. The *lines* indicate how the spinal canal angle (*SCa*) on both sides was determined. *SCa* is the angle between the coronal plane and the line connecting the most posterior point of the spinal canal and the junction of the spinal canal and neurocentral junction. **a** Immediately postoperative CT image. **b** Same as **a**, but zoomed in. **c** CT scans 7 months postoperatively

L2 angles at the 7-month follow-up; and (3) the difference in the normalised L2 angles at these two time-points.

The data were analysed using Statview 5.0 (SAS Institute Inc., San Francisco, CA, USA).

Statistical significance was accepted at the $P < 0.05$ level.

Results

Three animals died during the study (2 deaths related to anesthesia, 1 death due to infection unrelated to surgery). At the end of the 7-month follow-up, 10 pigs had survived and were available for the final CT examination.

The animals had been allowed to mix with other members of the herd not participating in the study and upon observation, there were no visible differences in their gait or appearance. This led us to conclude that none of the animals had any apparent neurological disturbances.

The CT scans taken immediately after surgery revealed that the screws penetrated the neurocentral junction perpendicularly and occupied almost the entire pedicle as planned. All 13 screws were positioned correctly.

The values for the spinal canal (SCa) and vertebral body (VBa) angles, measured immediately following surgery and at the 7-month follow-up, are shown in Table 1.

There was no significant difference between the screw and non-screw sides for the normalised spinal canal SCa angles at the intraoperative or 7-month follow-up assessments ($p > 0.05$). The reduction in normalised angle between the intraoperative and 7-month assessments (last column in table) was slightly greater on the screw side than the non-screw side but the difference was not significant ($p = 0.24$).

There was no significant difference between the screw and non-screw sides for the normalised vertebral body VBa angles at the intraoperative assessment ($p = 0.96$). However, at the 7-month follow-up assessment, the side difference was significant ($p = 0.005$). The change in normalised angle from intraoperative to 7 months later was significantly different between the screw and non-screw sides ($p = 0.009$): the normalised angle had reduced on the non-screw side but increased on the screw side, indicating asymmetry in the vertebral body growth. This alteration in the development of the vertebral body is clearly visible in the form of asymmetry, whereas the spinal canal cross-sectional area remained symmetrically elliptic in shape (Fig. 3).

Discussion

There is little data regarding the effect of pedicle screws on the growth of the spine. Most spinal surgeons have some reservations about using pedicle screws in the paediatric patient population, especially in very young patients, because they assume that pedicle screws passing through the neurocentral junction might alter the growth of the spinal canal. Our study results showed, however, that this fear might be unsubstantiated. It would appear that pedicle screws placed in the immature spine do not have a significant negative effect on the development of the spinal canal.

The neurocentral junction is situated at the junction of the vertebral body and the pedicles. It is situated inside the

Table 1 Spinal canal and vertebral body angles for the screw and non-screw sides at L2 and L3, measured immediately postoperatively and at 7 months follow-up

Dimension	Side	Intraoperative			7 months follow-up			Intraop minus 7 months follow-up
		L2 mean	L3 mean	L2 normalised to L3	L2 mean	L3 mean	L2 normalised to L3	L2 normalised to L3 value
Spinal canal angle (deg)	Non-screw	66.0 (7.1)	67.0 (6.3)	**0.985** (0.064)	71.4 (3.7)	74.3 (4.0)	**0.962** (0.037)	**0.023** (0.056)
	Screw	67.8 (4.4)	67.5 (3.5)	**1.005** (0.051)	64.9 (4.7)	69.6 (5.6)	**0.935** (0.075)	**0.070** (0.090)
	Non-screw versus screw			$P = 0.96$			$P = 0.14$	$P = 0.24$
Vertebral body angle (deg)	Non-screw	77.7 (4.5)	77.5 (4.7)	**1.003** (0.034)	69.2 (4.9)	75.7 (4.2)	**0.914** (0.027)	**0.088** (0.026)
	Screw	73.5 (5.8)	73.1 (4.8)	**1.005** (0.064)	84.7 (4.0)	82.3 (3.8)	**1.030** (0.044)	**−0.025** (0.080)
	Non-screw versus screw			$P = 0.96$			$P = 0.005$	$P = 0.009$

Numbers in bold indicate the calculated normalised values

definitive vertebral body as defined in descriptive anatomy [9]. Neurocentral cartilage progressively moves posteriorly because of the fact that it contributes more to the growth of the posterior portion of the vertebral body than to the growth of the posterior arch [10]. Growth is most active in the years up to age 5 and soon after that (usually between 3 and 6 years of age), the neurocentral junction fuses [9, 11]. Pedicle screw constructs are frequently used in the treatment of adolescent and sometimes also juvenile idiopathic scoliosis without any obvious late effects manifest as spinal stenosis. The question, however, is whether they are also safe in younger patients, where the neurocentral junction is not fused and is indeed still active (aged 4–6 years of age). Ruf and Harms reported that the placement of pedicle screws in children of 1–2 years of age does not result in spinal canal stenosis, although their follow-up for the majority of patients was only 2 years [12]. In order to assess the clinical effect of pedicle screws in terms of spinal canal dimensions, a study would be needed in which patients are followed-up until at least skeletal maturity. Hence, a follow up period of at least 10–15 years would be required to identify any clinically significant spinal stenosis.

An option to obviate the problem of long follow-up is the use of animal models. One of the most suitable in vivo models is that of domestic pigs, because they most closely approximate the human vertebrae in terms of size and shape [13]. In addition, they are bred to grow quickly, and this high speed of growth renders them a suitable model to perform studies over a short time-span. Porcine models with pedicle screws were initially used to study the development of scoliosis [6, 14]. The data in the literature regarding the effect of pedicle screws on the growth of the vertebrae in porcine models are controversial. The first study reporting spinal canal stenosis due to the application of bilateral screws in the pedicles of pigs was published in 1961 [15]. Zhang and Sucato examined the effect of one sided epiphysiodesis with pedicle screws in the thoracic spine on 8 levels [3]. One of their findings was that the spinal canal cross sectional area in the adult animals was not decreased after insertion of pedicle screws in the immature spine, although their study was actually tailored to examine the effects on spinal alignment. Furthermore, even in their control group there was some surgical exposure, which might have disturbed the growth of the posterior elements and hence influenced the development of the spinal canal.

Others, (Cil at al. [2]) have reported a significant disturbance of spinal canal growth after the insertion of pedicle screws in the immature lumbar spine of domestic pigs. These authors explained that, in making their measurements, they divided the canal into 2 hemi-canals, with a sagittal line passing through the entry point of the basivertebral vein into the corpus (which was considered the

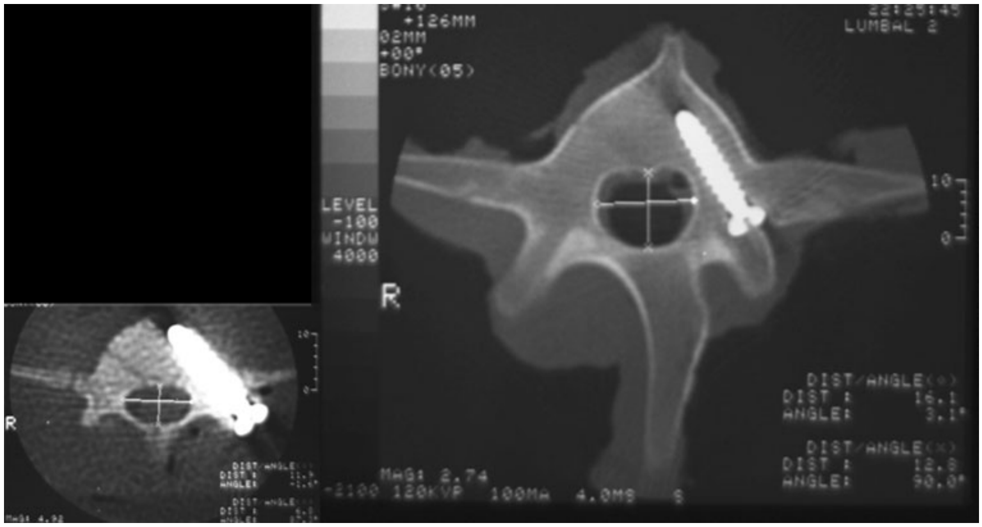

Fig. 3 Axial CT scan at the L2 level immediately postoperatively (*small inset*) shows the unilateral pedicle screw occupying almost the entire neurocentral junction (NCJ) and the pedicle. 7 months later there is an obvious deformation of the vertebral body. Note the eccentric location (shifted towards the screw side) of the anterior vertebral body crista. No alteration in the symmetry of the spinal canal is visible

midpoint) and the pointed midpoint of the anterior aspect of the corpus of the vertebra. The dividing line was hence arbitrarily defined with reference to the vertebral body. However, our results showed that pedicle screws have a significant effect on vertebral body growth, causing deformation in the axial plane, which would serve to challenge the validity of this measure. Furthermore, the neurocentral junction contributes more to the growth of the vertebral body than to the posterior arch, such that its disruption causes vertebral body distortion rather than canal stenosis [10]. We therefore contend that the difference between the two hemi-canals reported in the study of Cil et al. [2] reflects vertebral body asymmetry rather than spinal canal asymmetry. The same argument applies to their measurements of pedicle length. Their method here also included the vertebral body dimensions in the axial plane, although the vertebral body was itself distorted. Their result is even more surprising if one considers that in their porcine model there was only a fourfold increase in body weight by the end of the study.

The aforementioned studies examining the effect of pedicle screws on spinal growth all instrumented several spinal levels. This necessitates a long dissection, and a relatively large approach, which accentuates the possible approach-related growth disturbance. Furthermore, instrumenting more levels unilaterally usually causes a deformity, which in turn might influence vertebral body growth per se. In our study, we used only a single screw in each pig and our approach was very small such that these potential confounding factors were minimized. This allowed examination of the unique role of the neurocentral junction in the vertebral development/growth. However, the design with only a single pedicle screw also has its limitations. In few cases of EOSD would a single pedicle screw be sufficient for treatment, and we cannot predict what the cumulative effect of multiple screws might be. This should be further investigated in multisegmental animal models. In addition, as with all animal studies, care must be taken when translating the conclusions to the treatment of humans.

In summary, in this study, a single pedicle screw inserted through the active neurocentral cartilage in immature pigs caused significant distortion of the vertebral body, but did not result in significant deformation of the spinal canal compared with control levels.

Conclusion

Pedicle screws had a significant effect on the growth of the vertebral bodies in the axial plane, but there was no significant effect on the spinal canal. Our results provide further support for the existing arguments in favour of pedicle screws when weighing up the many factors to be considered in creating a treatment plan for early onset scoliosis.

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Conflict of interest None.

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