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General Articles

Surgical repair of rib fractures in 14 neonatal foals: case selection, surgical technique and results

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Summary

***Reasons for performing study*: Fractured ribs are encountered quite frequently in newborn Thoroughbred foals, often with fatal outcome. Surgical repair of fractures therefore requires consideration as a means of reducing mortality.**

***Objectives*: To evaluate the repair of rib fractures using internal fixation techniques in foals at 2 different equine hospitals following similar diagnostics and case selection.**

***Methods*: The records of 14 foals that underwent internal fixation of fracture ribs were reviewed. Subject details, clinical presentation, diagnosis, surgical technique, post operative care and complications were recorded. Follow-up information was obtained in 7 foals.**

***Results*: The fractured ribs were reduced and stabilised using reconstruction plate(s), self-tapping cortical screws and cerclage wire in 12 cases, Steinmann pins and cerclage wires in 1 case and both techniques in 1 case. Not every rib was reduced on each case. Surgical reduction was performed on an average of 2 ribs, range 1–3 ribs in each foal. At the time of writing, 4 foals had been sold, one age 2 years was in training and 2 others died from unrelated causes.**

***Conclusions*: Our data support the use of surgical stabilisation utilising reconstruction plates, self-tapping cortical screws and cerclage wire for selected cases of thoracic trauma in neonatal foals. The use of Steinmann pins may be suboptimal due to cyclic failure, implant migration and the potential for iatrogenic internal thoracic trauma.**

***Potential relevance*: Foals with existing extensive internal thoracic trauma resulting from rib fracture(s), or the potential for such trauma, previously considered to have a guarded to poor prognosis for survival, may be successfully managed with internal fixation of selected fracture sites.**

Introduction

Myocardial lacerations or punctures caused by fractured ribs are consistently fatal events (Sprayberry *et al*. 2001) and sudden death can occur without any previously identified clinical signs (Schambourg *et al*. 2003). In a study of 760 necropsied neonates, 19 of the 76 foals diagnosed with rib fractures died as a direct result of rib trauma (Schambourg *et al*. 2003). Rib fractures were also an important contributor of morbidity and mortality in 56 foals presented to a referral practice in Kentucky. Of the 27 foals that died after referral, 14 succumbed as a direct result of complications attributable to their fractures, including pulmonary contusion, haemothorax, pneumothorax, diaphragmatic herniation, haemoabdomen, haemopericardium and myocardial laceration (Figs 1–3). The same study alluded to the survival of 2 foals with multiple rib fractures following internal fixation of the affected ribs; 10 of 11 foals with similar fractures not surgically treated died (Sprayberry *et al*. 2001). However, at one Thoroughbred studfarm in Ireland, 20% of the season's crop of 263 neonates showed thoracic asymmetry and trauma, and 5 foals had rib fractures identified on radiographic examination, but none were reported to have developed associated complications (Jean *et al*. 1999).

Most commonly, treatment recommendations for foals with rib fractures include box rest and supportive care as needed. Specific treatment protocols are based on the degree of internal thoracic injury and may include thoracocentesis, oxygen supplementation, blood transfusion, i.v. fluids, antibiotics, analgesics and anti-inflammatory therapy (Byars 1997). Specific recommendations for surgical intervention have not been reported. The purpose of this study was to describe and evaluate methods of internal fixation for rib fractures based on our experience treating 14 neonatal foals with existing internal thoracic trauma or at high risk of sustaining such injury.

Materials and methods

The medical records of 14 foals with rib fractures treated by internal fixation were selected from a group of 68 foals referred with a presenting diagnosis of fractured ribs, or in which the fractures were diagnosed on initial evaluation. Information obtained from each record included subject details, clinical presentation, diagnosis, surgical technique, post operative care and complications. For the foals that died or were subjected to

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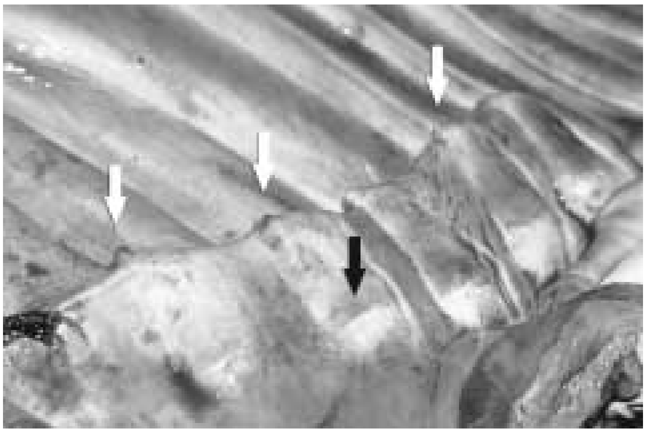

Fig 1: Fractured ribs in a foal age 48 h that suffered sudden death. Note the sharp edges of the distal fragment (white arrows), and the proximal location of the fracture in relationship with the costochondral junction (black arrow). This foal was not included in the study.

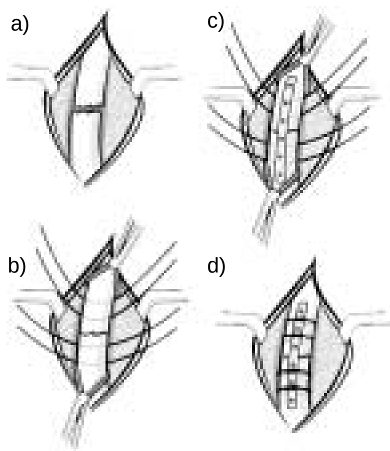

Fig 2: Line drawing of the most utilised surgical technique. Note the sequence of events illustrated by: a) displaced rib fracture; b) fracture reduced with the use of towel clamps placed proximally and distally, along with preplaced cerclage wires; c) placement of the reconstruction plate; and d) cerclage wires tightened in a single loop pattern proximally and distally to the fracture line, over the reconstruction plate.

euthanasia, the cause of death or reason for euthanasia was obtained from the necropsy records. Survival information was obtained by telephone conversation with the owner, farm manager, or referring veterinarian.

Case selection

Foals with rib fractures present with clinical signs that vary from subtle respiratory and systemic abnormalities to obvious distress. Fast and shallow breathing with increased abdominal effort, lethargy, prolonged recumbency and stiffness while walking are common. In the present study, bilateral synchronous palpation of the rib cage was completed in all foals. Thoracic asymmetry with the presence of subcutaneous oedema was present in all 14 foals and was regarded as highly suggestive of rib fracture, even when the fracture itself could not be palpated. Confirmation and characterisation of the fracture, as well as identification of secondary internal thoracic lesions, including lung consolidation, pleural effusion and pleural haemorrhage, was accomplished using ultrasonography. This method was utilised in all cases as the main diagnostic tool and provided invaluable information during case selection. Radiographs were not considered as valuable as a diagnostic method. This was based on the authors' experience and on the previously reported poor correlation between radiographic evidence and presence of fractured ribs (Jean *et al*. 1999).

Fig 3: Intraoperative photograph of the reconstruction plate (arrowhead) with preplaced cerclage wires (white arrows); this was the most common technique utilised in this group of foals.

In the current study, internal fixation was performed in cases with confirmed severe internal thoracic injury (n = 6), or in cases where the potential for such injury was present (n = 8) (Table 1). The potential for internal thoracic injury was considered probable in foals that had 2 or more complete fractured ribs with axial deviation of the fracture extremities, particularly those located over the heart. Therefore, stabilisation of the fractures adjacent to the heart, and/or those identified as responsible for internal thoracic injury, was the principal objective of repair.

Surgical technique

Anaesthesia protocol for foals with a stable cardiovascular status consisted of sedation and muscular relaxation with diazepam[1] 0.04–0.10 mg/kg bwt i.v., induction with ketamine (Ketaset)[2] 1.5–2.2 mg/kg bwt i.v. and maintenance with the gaseous agent isoflurane[3] in a semiclosed flow circuit. For the less stable individuals, muscle relaxation and sedation with diazepam followed by gaseous induction and maintenance with isoflurane was the protocol utilised. Intermittent positive pressure ventilation was required in only 2 foals that had loss of negative intrapleural pressure.

Once anaesthetised, the foals were placed in lateral recumbency with the injured ribcage uppermost and the thoracic limbs extended as cranially as possible to facilitate exposure of the craniovental thorax. The surgical site was prepared routinely and draped for aseptic surgery.

After identification of the fracture sites by digital palpation, a 10–15 cm dorsoventral incision was performed over the most centrally located affected rib. When fracture reduction of more than one rib was necessary, the incision was centred to allow

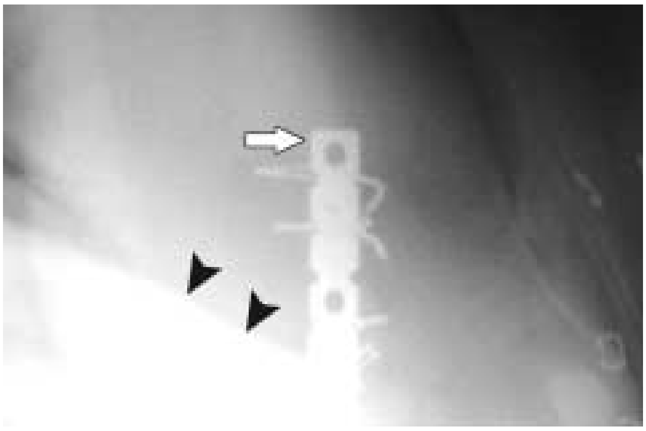

Fig 4: Post operative radiograph showing the reconstruction plate and cerclage wires (white arrow). Note the caudal aspect of the distal humerus (black arrowheads).

exposure of at least 2 or 3 ribs after soft tissue retraction. When necessary, a second dorsoventral incision was completed parallel and at a suitable distance cranially or caudally to the initial incision. The skin incision was extended through the cutaneus *trunci* muscle and, following retraction of the *lattisimus dorsi* muscle, the *serratus ventralis* muscle was dissected bluntly to expose the affected rib. Fracture reduction and reapposition of the ribs was accomplished using small bone forceps or towel clamps.

A 2.7 mm reconstruction plate[4] was contoured to each rib(s). The plate length was selected to allow for at least 4–6 cortices of fixation per side. Plates were applied with 2.7 mm diameter fully threaded self-tapping cortical screws[4] engaging both cortices of either the proximal or distal fragment. Lastly, orthopaedic wire (18–22 gauge) was placed to encircle the rib and the plate at 2 sites above and 2 sites below the fracture (Figs 2, 3 and 4). There were 3 exceptions to the above-described technique. In *Case 1*, 2 contoured Steinmann pins (2.0 mm diameter) were placed and secured at the outer border of the rib with cerclage wires for fracture reduction. In *Case 14*, 2 reconstruction plates were applied with fully threaded cortical screws, without cerclage wire application. In *Case 13*, a combination of 2 techniques was utilised, in which one rib was reduced with Steinmann pins and cerclage wires, and another 2 ribs were reduced with the use of reconstruction plates, cortical screws and cerclage wire.

Apposition of the musculature and skin were performed routinely. A 9 x 6 mm Penrose drain was placed in the subcutaneous space of several cases to minimise the risk of seroma formation. Where necessary, to re-establish intrapleural negative pressure, a blunt trocar attached to suction tubing was introduced through the intercostal space prior to skin closure. In *Case 14*, a foal with marked thoracic wall damage, an active intrathoracic drain (Jackson-Pratt)[5] was placed prior to soft tissue apposition, to facilitate post operative care.

Post operative care

Post operatively, the foals were monitored for attitude, respiratory distress and degree of comfort. Monitoring of respiratory status was accomplished by physical examination and blood gas analysis. Most of the foals were kept in sternal recumbency, with a slight inclination towards the nonaffected hemithorax, in order to minimise stress over the surgical site. This was accomplished with a V-shaped support and padding. Pleural fluid was removed by continuous suction drainage in one foal, and as needed in the remaining foals during the first 72 h. All subcutaneous drains were removed by 72 h. All foals were given ketoprofen (Ketofen)[2] 2.2 mg/kg bwt i.v. or flunixin meglumine (Banamine)[6] 1.1 mg/kg bwt i.v. and antimicrobial drugs pre- and post operatively. Rifampin (Rifadin)[7] 5 mg/kg bwt *per os* and sulphamethoxazole/ trimethoprin (Bactrim)[8] 30 mg/kg bwt *per os* were administered most commonly. Analgesic and anti-inflammatory agents were reduced or discontinued in an attempt to discourage excessive activity and avoid potential failure of the implants, soon after the foals became ambulatory.

Box rest was recommended for a total of 4–6 weeks. Ultrasonographic evaluation of the fractured sites was performed every 2 weeks, until healing was observed and deemed sufficient to allow regular turnout.

Results

The study population included 13 Thoroughbreds and 1 Standardbred. Age at the time of surgery was 1 h to 5 days, with 3 foals age <12 h, 4 foals between 12–24 h and 6 foals >24 h. There were 10 males and 4 females. Respiratory distress was the most common presenting clinical sign. Only 7 foals were referred with the primary complaint of rib fracture. In the others, rib fractures were identified during the initial physical examination, which included synchronous palpation of the left and right hemithoraces, followed by ultrasound evaluation.

Rib fracture location and classification were similar in most foals. The exact number of broken ribs per foal (range 3–7) was listed in only 8 records but, in the remainder, multiple fractures were documented. Fractures were located at (n = 2) or within 4 cm proximal to (n = 8) the costo-chondral junction in 10 foals; location was not reported in 4 foals. More foals had fractures involving the left hemithorax (n = 10) and all foals had complete fractures with axial displacement of the distal fragment towards the heart. Evidence of internal thoracic injury was documented at the time of presentation in 6 of these cases (Table 1). Rib fracture displacement was most common with fractures involving the 4th, 5th and 6th ribs. The presence of a flail chest was reported in only one foal (*Case 2*).

Although each foal had at least 2 fractured ribs, not all ribs were reduced surgically (Table 1). A single rib repair was performed in one foal with 3 rib fractures, while most other cases had 2 (n = 9) or 3 (n = 4) ribs surgically stabilised. Fractures of the 3rd, 4th, 5th and 6th ribs were those most commonly repaired, with the 4th and 5th rib being the most frequently reduced pair.

The total number of rib fractures repaired was 31. Seventeen ribs were repaired using 4-hole 2.7 mm reconstruction plates, cortical screws and cerclage wires; 11 ribs were repaired using 6-hole 2.7 mm reconstruction plates, 2 of which were without cerclage wires. Three ribs were repaired only with Steinmann pins and wire. (Table 1). Mean surgery time was 1 h, ranging from 55–100 mins. Implant failure was recorded in 3 ribs; 2 following Steinmann pin reduction (*Case 1*), and one with a reconstruction plate without cerclage wire (*Case 14*).

In addition to implant failure, which was fatal in one case, other post operative complications included diffuse swelling, seroma formation and subcutaneous haematoma, which were observed in 6 foals. No post operative complications occurred in 7 foals. The mean duration of hospitalisation was 6.7 days (range 2–25 days).

TABLE 1: Summary of the criteria for case selection, surgical technique and complications

Foal	No. fractured ribs	Fracture type	Signs of internal thoracic trauma	Surgical technique	No. ribs reduced	Surgical complications
1	Multiple	CAD	PC/PB/PN/HM	ST/W	2	Implant failure
2	7	CAD	None	RCP/W	2	None
3	4	CAD	PB	RCP/W	3	None
4	4	CAD	None	RCP/W	2	Oedema/seroma
5	3	CAD	None	RCP/W	2	None
6	Multiple	CAD	None	RCP/W	2	None
7	Multiple	CAD	PC/PB/PN/HM	RCP/W	3	Seroma/PN/drainage
8	3	CAD	None	RCP/W	1	None
9	4	CAD	PC/PN	RCP/W	3	None
10	6	CAD	PC/PN/HM	RCP/W	2	Seroma
11	Multiple	CAD	None	RCP/W	2	Pressure sores
12	6	CAD	None	RCP/W	3	Oedema/seroma
13	Multiple	CAD	None	ST/RCP/W	2	Oedema/haematoma
14	Multiple	CAD	PC/PN/HM	RCP	2	Seroma/PN

CAD = Complete with axial displacement; PC = Pulmonary contusion; PB = Pericardial bruising; PN = Pneumothorax; HM = Haemothorax; ST = Steinmann pins; W = Cerclage wires; RCP = Reconstruction plate.

Of the 14 foals, 12 were discharged from the hospital. One died due to complications related to the surgery (*Case 1*) and a second was subjected to euthanasia due to severe *Clostridium perfringens* enterocolitis (*Case 12*). None of the implants in the foals that were discharged needed to be removed.

Follow-up information was obtained for 7 foals. Three were sold as yearlings, and one as a weanling, all apparently in good health. One other healthy 2-year-old was in training. Two horses died from unrelated causes.

Discussion

Rib fractures in foals occur most commonly in association with primiparous mares, and those who have suffered maternal- and/or fetal-related dystocia (Jean *et al*. 1999). The shape of the chest in Thoroughbred foals, retention of a flexed elbow causing focal pressure on the thoracic cage during parturition, narrower than usual pelvic canal, vagina and perineal structures, and excessive manipulation during assisted delivery have all been reported as contributing factors (Jean *et al*. 1999). In our group of 14 foals, 13 were Thoroughbreds, possibly reflecting the high population of this breed in the central Kentucky area. Of the 9 Thoroughbred foals in our study for which parturition history was available, 8 dystocias were documented. Sprayberry *et al*. (2001) reported an incidence of thoracic trauma in colts 3 times higher than in fillies. Colts were also the predominantly affected sex in this series. However, Schambourg *et al*. (2003) found no sex predilection, while Jean *et al*. (1999) observed fillies to be marginally but not significantly more affected than colts. This was attributed to a possible difference in thoracic cage compliance, since no difference in the thoracic circumference or weight between the 2 sexes was found. In the current study, it is uncertain why more males vs. female foals were involved.

In the current study, foals were selected for surgical management based on their existing internal thoracic injuries, or the potential for such injury to occur. This potential was based on the location and degree of displacement of the fragments. Seven foals were referred with a primary complaint of rib fractures; in the remaining foals, the fractures were identified during initial evaluation. Clinical signs varied; however, a mild to moderate degree of pain evidenced by increased respiratory effort, depression and reluctance to make sudden movements were consistent in all foals. These findings reinforced the conclusion that fractured ribs should be included as a differential diagnosis for all neonatal foals presenting with depression, respiratory distress and signs suggestive of pain.

Fracture location was recorded to be either at the costochondral junction or proximal to it in 10 foals in the present study. These findings are similar to those obtained in previous reports (Jean *et al*. 1999; Sprayberry *et al*. 2001; Schambourg *et al*. 2003). In our experience, complete fractures located proximal to the costochondral junction may present with different configurations. The fracture extremities can override and lacerate the intercostal muscles and vessels, and cause haematomas, periosteal damage and severe pain. Fragments displaced axially can perforate the parietal pleura, bruise or lacerate the heart, lungs and major vessels, and cause severe blood loss, hypovolaemic shock and death (Byars 1997). In our study, the selection criteria favoured cases with fragments in proximity to the heart. Rib fractures in neonatal foals are typically located in the cranial ventral half of the thorax (Jean *et al*. 1999; Schambourg *et al*. 2003).

In this study, foals presented with axially displaced fractures involving the 4th, 5th and 6th ribs of the left hemithorax were considered at greater risk of developing life-threatening injuries, and were most commonly subjected to surgery (n = 10). Dislocations through the costochondral junction may also cause internal thoracic injury, as was evident in 2 foals included in this study. Both foals developed pulmonary contusion, pericardial bruising and haemothorax. Therefore, costochondral junction dislocations should not be disregarded as a potential life-threatening condition.

Surgical intervention for the treatment of human patients with flail chest has gained acceptance over the last decade. Advantages are documented in a recent study (Tanaka *et al.* 2002), which compared surgical stabilisation of the chest wall to conservative therapy (pneumatic stabilisation) in selected human patients with flail chest. Patients that underwent surgery required less time on ventilation, had a lower incidence of pneumonia, required fewer days in intensive care, had lower medical costs, and were able to return to full work more quickly (Tanaka *et al*. 2002). Similarly, in the present study, all foals showed a substantial subjective improvement in their level of comfort post operatively in comparison with preoperative observations. When compared to foals with rib fractures not undergoing surgical stabilisation, outcome also appears improved, although cases were not matched for degree of injury (Table 2).

TABLE 2: Quantification of the caseload, types of treatment and their outcome during the study period

Year	Cases	Type of treatment		Cons outcome			Surgical		
		Cons	Surgical	Died	Eut	D/H	Died	Eut	D/H
1999	9	8	1	4	2	2	1	0	0
2000	31	27	4	13	4	10	0	0	4
2001	18	14	4	7	0	7	0	0	4
2002	10	5	5	3	2	0	0	1	4
Total	68	54	14	27	8	19	1	1	12
Mortality*				45.3%			7.1%		

*Mortality numbers exclude foals that died or were subjected to euthanasia due to unrelated causes; Cons = Conservative; Eut = Euthanasia; D/H = Discharged from hospital.

A variety of surgical techniques for stabilisation of flail chest in man have been reported, including external towel clamp traction, application of overlapping rib struts, intramedullary wiring, fracture reduction using absorbable suture, and insertion of a removable ‘sea gull’ wing prosthesis. Oyarzun *et al* (1998) reported the successful use of 3.5 mm acetabular reconstruction plates with cortical screws. Reported advantages included safety for patients and surgeons, complete soft tissue coverage of the implants, implant removal not required, and elimination of neurovascular bundle pain secondary to cerclage wire placement. In this study group of 14 foals, the first attempt at internal fixation was performed by securing Steinmann pins contoured to the outer border of the rib with cerclage wires. Three days post operatively, the foal’s condition started to deteriorate rapidly and the animal died. Necropsy findings revealed that one of the Steinmann pins had broken and migrated into the chest, causing further damage to the heart. Cyclic failure of the Steinmann pin was suspected. As a result, the utilisation of reconstruction plates instead of Steinmann pins to support the outer border of the fractured ribs was considered. Reconstruction plates are malleable, can readily be shaped and trimmed to length to support fractures having complex surfaces, and allow secure placement of the cerclage wires within its grooves, providing additional stability and protection against cyclic pullout of the screws. Furthermore, in our experience, the use of 4-hole plates with cerclage wires was adequate in most cases, providing sufficient strength and stability.

In 26 of the 31 repaired ribs, a combination of reconstruction plates, cortical screws and cerclage wires was utilised. Implant failure was recorded in one of 2 additional ribs repaired without the use of cerclage wire. The failure, in which pullout of the cortical screws from one of the proximal fragments occurred, was probably the result of excessive activity of the foal, which was inadvertently turned out into a small paddock 4 days post operatively. Our experience infers that the application of cerclage wires may have prevented this complication. A reported disadvantage of cerclage wires used for rib fracture stabilisation in human patients is neurovascular bundle pain; however, we did not recognise this complication in our group of foals.

The number of ribs fractured has been reported to be an indicator of a poorer prognosis in foals, cats and man (Kraje *et al*. 2000; Sprayberry *et al*. 2001; Sirmali *et al*. 2003). Schambourg *et al*. (2003) found that all life-threatening fractures involved 3 or more ribs. In man, stabilisation of only the ‘pillar ribs’ (4th to 8th) has been reported as sufficient for patients with flail chest (Reber *et al*. 1993; Reber 1998). Our results suggest that this is also true in foals. In the current study, multiple fractured ribs were observed in all foals; however, stabilisation of the fractures adjacent to the heart, and/or those identified as responsible for internal thoracic injury was the principal objective of the repair. For instance, in a case where the displaced fractured ribs identified were the 3rd, 4th, 5th and 6th, the ones closer to the heart, 4th and 5th, were reduced. This was the reason why 9 out of 14 foals had only 2 fractured ribs reduced. This approach provided enough stability to eliminate ongoing internal thoracic injury and re-establish satisfactory thoracic wall function.

The appropriate manner in which to position foals with fractured ribs is controversial. For those not yet taken to surgery, Byars (1997) recommended maintaining the affected side down, avoiding potential compression of the unaffected lung and allowing better gas exchange. This may, however, lead to intrathoracic damage if axial displacement of the fracture is present. In our experience, such cases call for early surgical intervention. In the post operative period, we opted to pursue sternal recumbency with a slight inclination towards the unaffected hemithorax. This orientation was intended to reduce stress over the surgical site and concomitantly minimise potential compromise of the unaffected lung. Complications associated with this choice were not recognised.

In man, Lardinois *et al*. (2001) reported post operative complications in 18% of patients undergoing chest wall stabilisation including atelectasis and pneumonia of the ipsilateral lung, myocardial infarction and wound infection. These complications were correlated strongly with the severity of the preoperative state of the individual patient. In the current study, besides the failure of the internal fixation with Steinmann pins, complications were comparatively minor, and included seroma formation and mild to moderate pleural effusion. Based on our findings, accumulation of large volumes of pleural effusion was an uncommon complication which was not directly correlated with the number of fractured ribs that were repaired.

An additional concern is whether implants in the girth region might be a cause of discomfort for horses under saddle. Our limited follow-up period and number of horses with follow-up data prevents us from drawing any definitive conclusions in this regard, although we anticipate that animals should be pain-free since the implants become incorporated within the body of the rib as the foals grow. None of the implants from the foals that were discharged needed to be removed.

The usage of nonsteroidal analgesic drugs was initiated preoperatively and tailored on an individual basis. In our study, the foal’s comfort level was usually improved subjectively after stabilisation of the thoracic wall. Wherever possible, analgesics were discontinued soon after the foals were ambulatory, in an attempt to discourage excessive activity to preserve the stability of the implants. The convalescence period was dictated by the rate of callus formation, which was best observed with the use of biweekly ultrasound evaluation.

In summary, internal fixation of rib fractures in foals using reconstruction plates, self-tapping cortical screws and orthopaedic cerclage wire is technically straightforward. The procedure facilitates healing by successfully resisting fracture displacement, thereby reducing pain and reducing the risk of additional life-threatening intrathoracic injury. The repair of rib fractures using Steinmann pins may be suboptimal, due to cyclic failure, migration and the potential for iatrogenic thoracic trauma. Primary treatment goals include pain reduction, prevention and cessation of intrathoracic trauma and the return of satisfactory respiratory function. To achieve these goals in foals with multiple fractures, it is necessary to repair only a selected number of ribs, based on their degree of displacement and location.

Internal fixation can be an effective treatment option in foals that sustain severe thoracic trauma and have a poor prognosis for life. Further investigation is necessary in order to assess whether severe thoracic trauma sustained during or soon after birth would have any impact in the foal's future pulmonary function and performance, and to compare conservative vs. surgical treatment.

Manufacturers' addresses

[1]Elkins-Sinn Inc., Cherry Hill, New Jersey, USA.
[2]Fort Dodge Animal Health, Overland Park, Kansas, USA.
[3]Halocarbon Laboratories, River Edge, New Jersey, USA.
[4]Synthes, Paoli, Pennsylvania, USA.
[5]Alegiance Health Care Corporation, McGaw Park, Illinois, USA.
[6]Schering Plough Animal Health, Union, New Jersey, USA.
[7]Hoechst Marion Roussel, Bridgewater, New Jersey, USA.
[8]Hoffmann-La Roche Inc. (Roche), Nutley, New Jersey, USA.

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