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REVIEW ARTICLE

Prevalence of complications in neuromuscular scoliosis surgery: a literature meta-analysis from the past 15 years

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Abstract
Purpose Our objectives were primarily to review the published literature on complications in neuromuscular scoliosis (NMS) surgery and secondarily, by means of a meta-analysis, to determine the overall pooled rates (PR) of various complications associated with NMS surgery.
Methods PubMed and Embase databases were searched for studies reporting the outcomes and complications of NMS surgery, published from 1997 to May 2011. We focused on NMS as defined by the Scoliosis Research Society's classification. We measured the pooled estimate of the overall complication rates (PR) using a random effects meta-analytic model. This model considers both intra- and inter-study variation in calculating PR.
Results Systematic review and meta-analysis were performed for 68 cohort and case–control studies with a total of 15,218 NMS patients. Pulmonary complications were the most reported (PR = 22.71 %) followed by implant complications (PR = 12.51 %), infections (PR = 10.91 %), neurological complications (PR = 3.01 %) and pseudoarthrosis (PR = 1.88 %). Revision, removal and extension of implant had highest PR (7.87 %) followed by malplacement of the pedicle screws (4.81 %). Rates of individual studies have moderate to high variability. The studies were heterogeneous in methodology and outcome types, which are plausible explanations for the variability; sensitivity analysis with respect to age at surgery, sample size, publication year and diagnosis could also partly explain this variability. In regard to surgical complications affiliated with various surgical techniques in NMS, the level of evidence of published literature ranges between 2+ to 2−; the subsequent recommendations are level C.
Conclusion NMS patients have diverse and high complication rates after scoliosis surgery. High PRs of complications warrant more attention from the surgical community. Although the PR of all complications are affected by heterogeneity, they nevertheless provide valuable insights into the impact of methodological settings (sample size), patient characteristics (age at surgery), and continual advances in patient care on complication rates.

Keywords Neuromuscular scoliosis · Complications · Scoliosis surgery · Deformity surgery · Systematic review · Meta-analysis

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Introduction

Neuromuscular scoliosis (NMS) amplifies the complexity of surgical intervention. While scoliosis surgery promises improvement in functional level, cosmesis, respiratory status, pain, health status, and overall quality of life [1–6], it is also affiliated with a high risk of peri- and postoperative complications [7–10].

The high risk of complications arises because of concurrent risk factors from disease pathology and its associated co-morbidities [7, 11]. Patients with NMS have significantly higher rates of morbidity and mortality compared to other scoliosis etiologies [7]. A 2011 cohort reports complication rates as high as 17.9 % for NMS followed by 10.6 % for congenital and 6.3 % for idiopathic scoliosis (IS); mortality rates follow the same trend at 0.34 % for NMS to 0.02 % for IS [7]. Higher complication rates illustrate the fact that patients with NMS incur higher costs ($66,953 vs. $47,463), lengthier hospitalizations (9.2 vs. 6.1 days) and a greater number of total procedures (4.2 vs. 3.0) compared to children with IS [10].

The high risk of complications raises fiscal concerns about the benefits of scoliosis surgery in these patients [12]. In order to better understand the complexities of the relationship between benefits and complications, we propose a view of complications literature in two broad categories: (1) Patient-specific characteristics (cardiopulmonary–neurological status, degree of deformity, disease diagnosis, nutritional status and complications) and (2) Surgeon- and surgery-related preferences (extent of surgery, surgical approach, type of instrumentation). We expect that an analysis of patient-related factors will help in improving patient selection and evaluation of suitability for surgery as well as minimize the risk of complications. In addition, an analysis of surgery-related preferences would help both surgeon and patient to make informed choices. Interpretation of the two categories in combination could later facilitate the development of cost-benefit analysis of surgery and outcomes.

Recently, large database studies on complications of scoliosis surgery have been published [7, 9, 13, 14]. Although these studies benefit from large patient populations, they might be prone to underreporting. On the other hand, smaller patient series based on a thorough follow-up of the patients might reveal larger complication rates [7, 9]. Our meta-analysis utilizes studies with a diversity of sample sizes.

The primary aims of the current work were to systematically review the published literature regarding complications in NMS surgery; to determine the overall pooled estimates of rates (PR) of various complications associated with NMS surgery by means of analytical meta-analysis, and finally to perform a sensitivity analysis to discuss variability in PRs in terms of the above-mentioned patient- and surgery-related characteristics to facilitate a comprehensive understanding.

As complication rates can have a substantial impact on decisions regarding allocation of medical resources, we investigated complication rates following the use of newer spinal instrumentation (from the late 1990s) to reflect current clinical practice [15].

Methods

Search strategy

In order to list the available studies in PUBMED (advanced search) and EMBASE, an electronic search was conducted using controlled vocabulary and key word terms. For the review we defined NMS in accordance with the Scoliosis Research Society's classification [16]. The combination of key words and text word terms for diagnosis and complications such as neuromuscular scoliosis and pulmonary complications were used (Tables 1, 2). The time frame for the query was from 1 January 1997 to 31 May 2011. The search was limited to English language publications. A total of 992 records were identified through database search. Two independent reviewers assessed these records for the presence of relevant terms in titles and abstracts. After removing unrelated and overlapping results from the two databases, 429 records were localized. The reviewers identified 78 relevant articles. In cases of disagreement regarding inclusion at this stage, the entire text was analyzed to reach an agreement. The citations and reference lists of all these articles were also referred to for the purpose of obtaining cross references. Eighty-six full text articles were subsequently analyzed by the first author in agreement with the inclusion and exclusion criteria established for the review.

Retrospective and prospective cohort studies and case–control studies were included. Studies reporting and

Table 1 Literature search in PubMed: text words and mesh terms

Search words		Number of hits using text words and MeSH terms
Text words combination		Text words in Title and abstract
1	"Neuromuscular scoliosis" and "Complications"	248
2	"Neuromuscular scoliosis" and "Pulmonary Complications"	27
3	"Neuromuscular scoliosis" and "Neurological Complications"	10
4	"Neuromuscular scoliosis" and "Infections"	0
MeSH Terms combination		MeSH term
5	"Scoliosis/Surgery" [MAJR] and "Surgical wound infection/etiology" [MeSH term]	46
		Total = 331

Table 2 Literature search in Embase: text words and Emtree words

Text words in quick search		Number of hits
1	"Neuromuscular scoliosis" and "surgical complications" limit "English"	154
2	"Neuromuscular scoliosis" and "surgical complications"	98
Emtree terms added to advanced search		
1	"Scoliosis" and "neurological complications"	86
2	"Scoliosis" and "infection complications"	10
3	"Scoliosis" and "pneumonia" and "spine surgery"	42
4	"Pedicle Screw" and "scoliosis" and "postoperative complications"	78
5	"Pseudoarthrosis" and "scoliosis" and "spine surgery"	193
		Total = 661

elaborating on the complications of NMS surgery following the use of newer spinal instrumentation (since the late 1990s) were considered. We investigated the types and frequencies of these complications to reflect current clinical practice. Follow-up cohort studies had to have a minimum average follow-up of 1 year. Average follow-up in included studies ranged from 1 to 6.2 years. Details of the included studies are shown in Appendix 1. Characteristics of excluded studies are shown in Appendix 2. Studies listing complications not associated with surgery and reporting on a sample with a mean age of less than 10 years at the time of surgery were excluded. Multiple publications reporting the same group of patients along with case reports and case series were excluded. The review did not include unpublished literature, theses and commentaries, and retracted studies. Meta-analysis was performed on a total of 68 studies. Frequency distributions and summary statistics were calculated for the follow-up data on complications.

Data extraction and management

Information contained in the included articles pertaining to study design, sample size, surgical age, and instrumentation type (Appendix 1) was extracted.

Frequency of adverse effects and complications was categorized into 5 major groups: pulmonary complications, neurological complications, infections, implant-related complications and pseudoarthrosis. The complications detailed in the review adhered to the criteria classified by Hod-Feins et al. [17].

Statistical analysis

Because our review brings together clinically and methodologically diverse studies, we expected heterogeneity in results. Therefore, we used a random-effects analytical meta-analysis model to combine individual prevalence rates into a single pooled estimate (PR) of rate for all complications [18, 19]. Single pooled estimate of various estimates of concern (incidence rates, effect size, odds ratio, relative risk) is used to report results from meta-analysis [20–25]. The use of a pooled estimate of complication rate (PR) in our meta-analysis is justifiable on the grounds as it keeps us from relying on results from a single study, provides opportunity for small and insignificant results to contribute to the overall picture, and represents results of a large sample of patients [26]. The limitation with PR is that it is affected by the quality of the individual data; we believe that the optimal methodological selection of studies addressed this concern [26, 27]. Cochran Q and I^2 statistics were calculated to assess heterogeneity between studies [28]. Of these, I^2 statistic was used to quantify the extent to which the results are affected by heterogeneity. It describes the percentage of total variation across studies (inconsistency) due to heterogeneity and not due to chance.

Quality scoring for individual studies was not feasible; therefore, we extracted relevant study characteristics for exposure (surgery), outcome (complications), follow-up time, sample size and age at surgery, a priori, as potential sources of heterogeneity. Of these, we performed exploratory sensitivity analysis for age at surgery, sample size, diagnosis, and publication year for all the complication groups. Sensitivity analysis involved undertaking the meta- analysis under characteristics of "different age at surgery", "sample size", "diagnosis subtype", and "publication year" to determine if these explain the heterogeneity in PRs. All the statistical analyses were performed using STATA 11 for Windows.

Results

Pulmonary complications

Thirty-seven studies, with a total of 7,710 NMS patients, were included. A total of 849 complications were reported, mainly comprising pneumonia, pneumothorax, atelectasis, pleural effusion, prolonged mechanical ventilation and longer stay in intensive care unit (ICU).

Figure 1 depicts the overall PR of pulmonary complications as 22.71 % (CI = 18.83–26.60). Substantial

heterogeneity of PR was observed ($Q = 1{,}632.50$ at $p < 0.001$), with 97.8 % of the variation in PR attributable to heterogeneity. The rates of pulmonary complications among studies vary between 0.00 and 93.55 %. For many studies, precision was poor because of wide confidence intervals. PR from sensitivity analysis with respect to age (<13 years; 19.50 % and ≥13 years; 22.93 %) at surgery, sample sizes (0 < 50, 23.44 %; ≥ 50 < 100, 19.70 %; and ≥ 100, 23.30 %) and publication year (1997-01, 14.58 %; 2002-06, 21.85 %; 2007-11, 29.43 %) suggests no significant difference in complication rates compared to overall PR (22.71 %). A statistically non-significant increasing trend of complications with passing years is present (Figure 1a, supplement). Sensitivity analysis for diagnosis depicts significantly lower pulmonary complications in myelomeningocele (2.83 % at $p < 0.001$) compared to DMD (20.83 %), cerebral palsy (CP) (30.20 %), and overall (Figure 1b, supplement).

Neurological complications

Thirty-three studies, with a total of 7,369 NMS patients, were included. A total of 199 neurological complications were reported, mainly comprising neurological compromise with partial or complete recovery, sensory motor deficits, and complete and incomplete spinal cord deficit.

Figure 2 depicts the overall PR of neurological complications: 3.01 % (CI = 1.61–4.40). Substantial heterogeneity of PR was observed ($Q = 177.80$ at $p < 0.001$), with 82.0 % of the variation in PR attributable to heterogeneity. Rates of neurological complications among studies vary between 0.00 and 61.39 %. Sensitivity analysis suggests higher complication rates (15.1 %; $p < 0.001$) with age at surgery <13 years compared to overall PR. A high rate (6.20 %) was seen in studies with a sample size >100. A higher rate was also seen in the studies from the late 1990s (1997-01, 10.28 %) compared to the overall PR (Figure 2a, supplement). Sensitivity analysis with respect to diagnosis subgroups suggests that myelomeningocele patients have higher neurological complications (5.02 %) compared to CP (0.58 %) and overall (Figure 2b, supplement).

Infections

Fifty-eight studies, with a total of 14,098 NMS patients, were included. A total of 1,096 infection complications

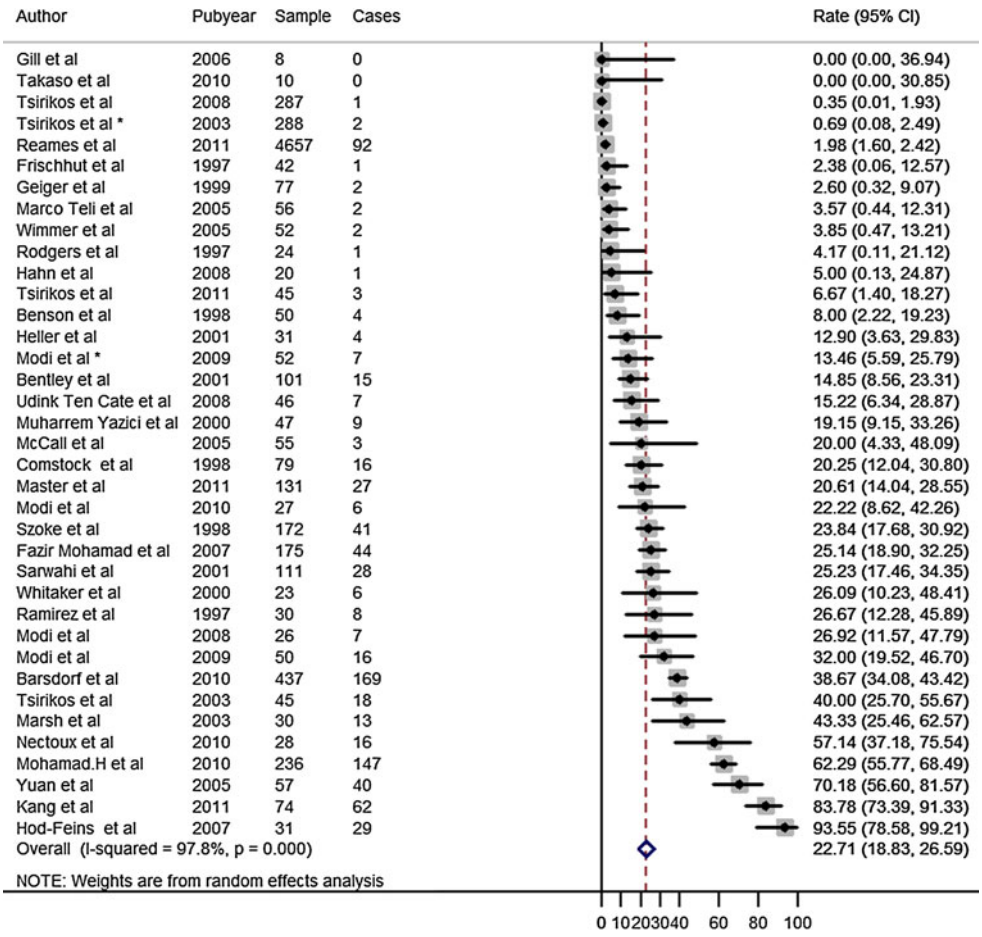

Fig. 1 Pulmonary complication

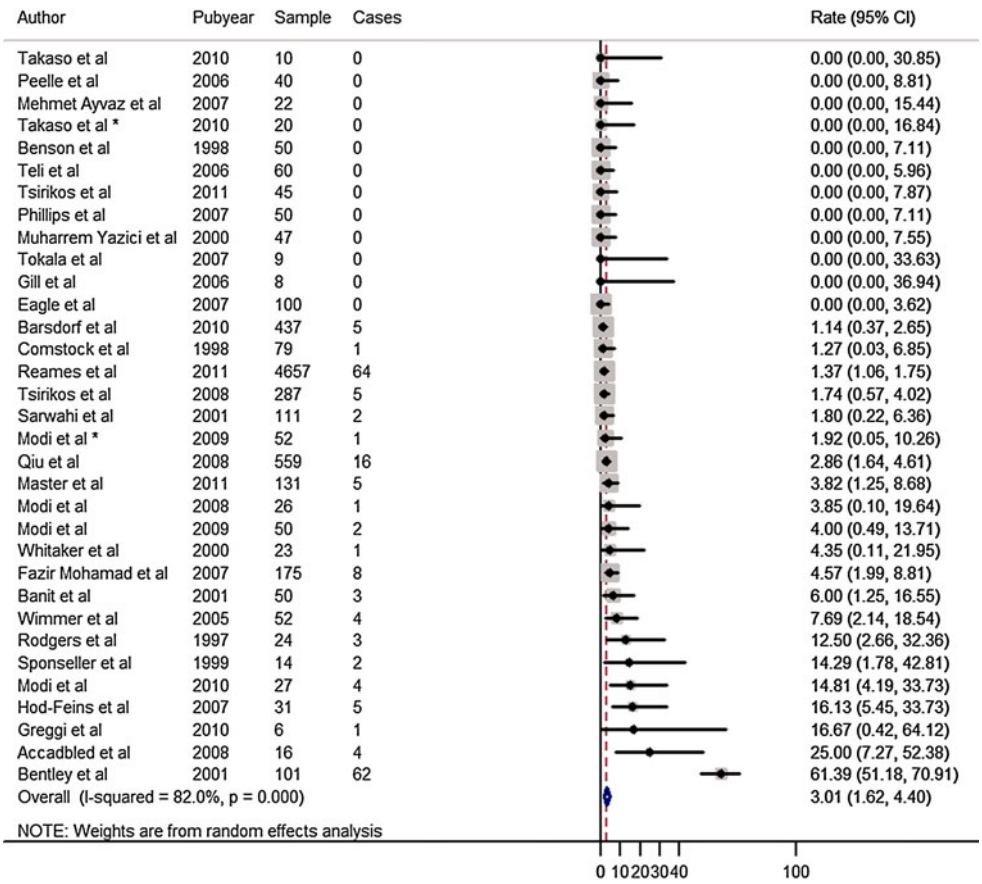

Fig. 2 Neurological complication

were reported; these included wound infections, decubitus ulcers, and chronic infection with delayed healing. Figure 3 depicts the overall PR of infection complications: 10.91 % (CI = 9.36–12.46). Substantial heterogeneity of PR was observed ($Q = 329.76$ at $p < 0.001$) with 82.7 % of the variations in PR attributable to heterogeneity. Rates of infection complications among the studies vary between 0.00 and 46.67 %. Infection rates from sensitivity analysis (age at surgery, sample size, publication year) were not significantly different from overall PR. Infection rates showed a statistically non-significant decreasing trend with increasing year of publication (1997–2001, 14.83; 2002–2006, 13.91; 2007–2011, 8.64 %) (Figure 3a, supplement). Infection rates in the myelomeningocele subgroup were significantly higher (20.32 % at $p < 0.001$) compared to DMD (6.96 %) and overall (Figure 3b, supplement).

Implant-related complications

Fifty-one studies, with a total of 7,612 NMS patients, were included. A total of 465 implant- related complications were reported; they included implant malplacement causing perforation and penetration, revision of implant for infection and skin irritation, implant breakage, loosening or cut-out of implant.

Figure 4 depicts the overall PR of implant-related complications: 12.51 % (CI = 9.82–15.20). Substantial heterogeneity of PR was observed ($Q = 350.18$ at $p < 0.001$) with 85.7 % of the variation in PR attributable to heterogeneity. Rates of implant complications among the studies vary from 0.00 to 66.67 %. Different age at surgery, publication year, and diagnosis type (Figure 4a, supplement; Figure 4b, supplement) had no effect on the rate of observed implant complications, whereas studies with a sample size >100 show low implant complication (6.54 %; $p < 0.001$) rates.

To facilitate clinical judgment, we categorized implant complications into malplacements, loosening, implant breakage, cutout/pullout/migration, implant removal, revisions, or extension (RRE), and implant prominence. Meta-analysis for these subcategories (Table 3) shows no evidence of significant heterogeneity, with variability across studies ranging from none to moderate. Cut-out/pullout/migration has the lowest PR of 2.38 % while RRE has the highest PR of 7.87 %.

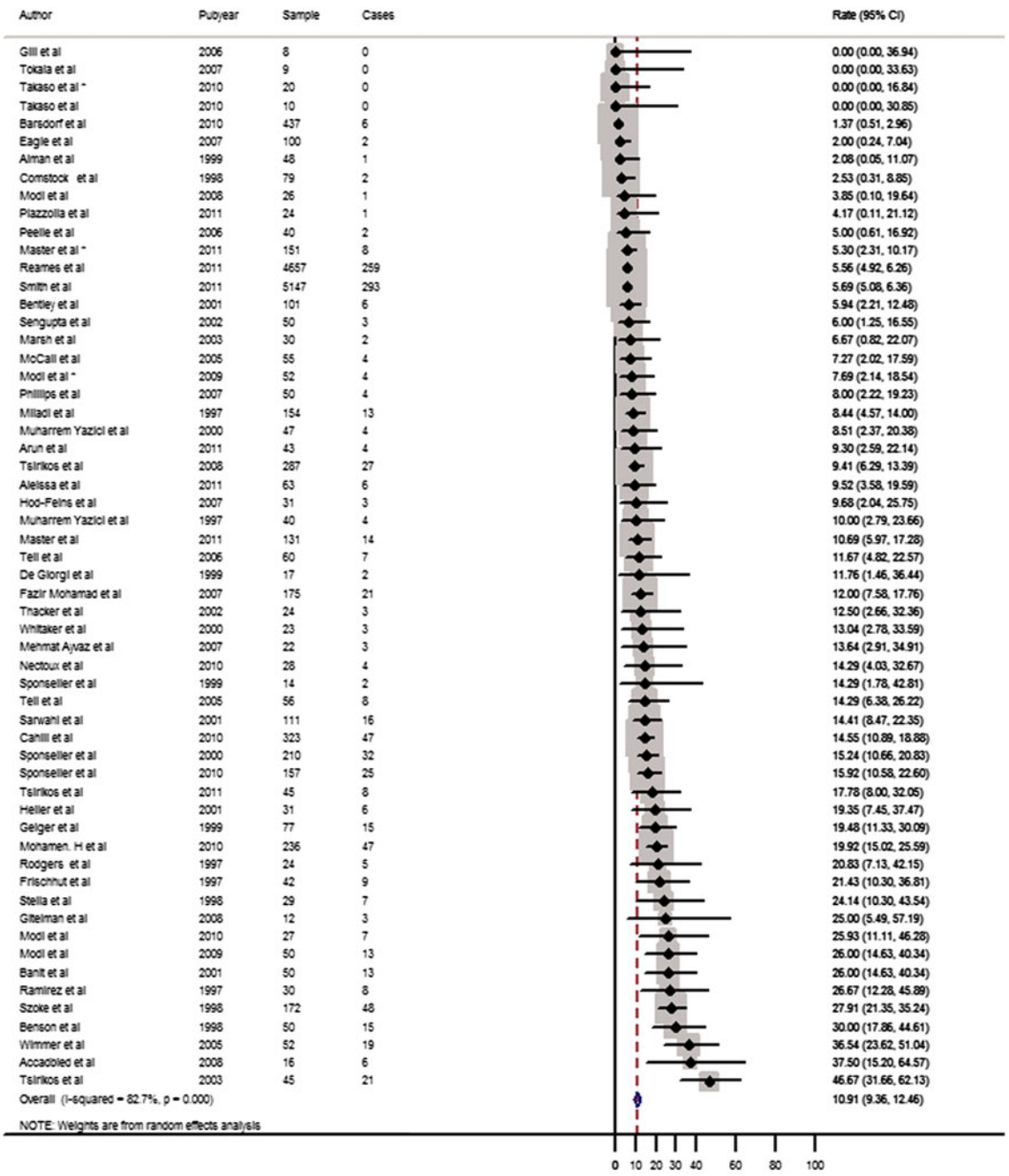

Fig. 3 Infections

Pseudoarthrosis

Thirty-three studies, with a total of 2,196 patients, were included. A total of 74 cases of pseudoarthrosis were reported. The included studies report the rates of pseudoarthrosis based on radiographic diagnosis.

Figure 5 depicts the overall PR of pseudoarthrosis: 1.88 % (CI = 0.90–2.86). Substantial heterogeneity of PR was observed ($Q = 53.65$ at $p \leq 0.001$) with 40.4 % of the variation in PR attributable to heterogeneity. Rate of pseudoarthrosis among the studies vary between 0.00 and 42.86 %. When operated at age <13 years, the pseudoarthrosis rate is significantly higher (11.64 %; $p < 0.001$) compared to the overall PR, with no such variation evident with sample size and publication year (Figure 5a, supplement). Pseudoarthrosis rates were significantly higher in myelomeningocele

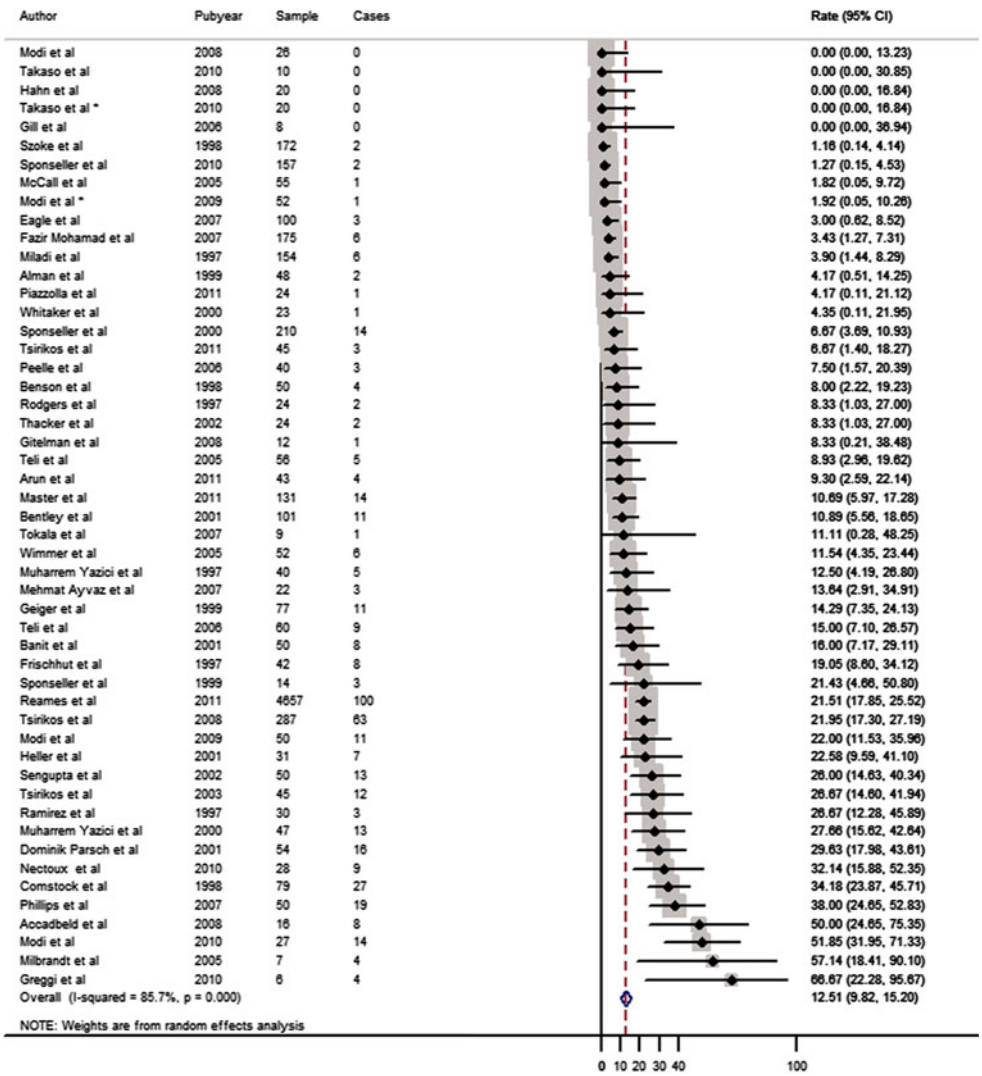

Fig. 4 Implant complication

Table 3 Subcategories of implant complications

	Implant complications	No. of studies	Pooled rate PR (%)	PR range in studies (%)	Cochran's Q	Variability across studies (I^2)
1	Malplacement	8	4.81	1.92–14.29	No	No
2	Loosening	16	2.39	1.14–22.22	No	No
3	Implant breakage	18	4.6	0.0–25	Yes	Moderate
4	Cutout/pullout/migration	4	2.38	1.27–13.33	No	Moderate
5	Removal/revisions/ extension	12	7.87	3.57–43.75	No	Moderate
6	Prominence	13	3.72	2.0–6.25	No	No

subgroup (12.63 % at $p < 0.001$) compared to CP (0.05 %), DMD (2.97) and overall PR (Figure 5b, supplement).

Our results show significant heterogeneity; PR for pulmonary complications is most affected by heterogeneity ($I^2 = 97.8$ %) in comparison to the remaining complication groups ($I^2 = 85.7$ %, implant complications; $I^2 = 82.7$ %, infections; $I^2 = 82.0$ %, neurological; $I^2 = 40.4$ % lowest for pseudoarthrosis).

Among the study characteristics, sensitivity analysis for age, sample size, publication year and diagnosis type suggest interesting trends of variation in the PRs, partially explaining the observed heterogeneity.

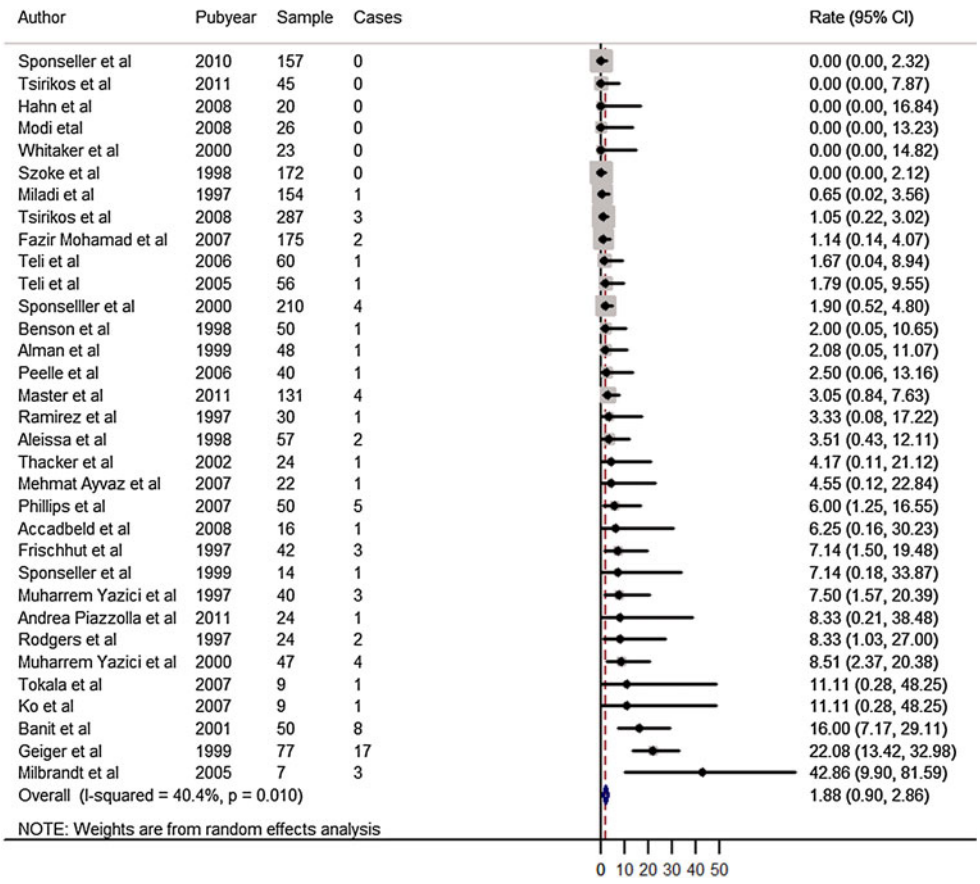

Fig. 5 Pseudoarthrosis

Discussion

The diagnosis of NMS itself is the most significant risk factor for peri-and postoperative complications [11, 29, 30]. NMS is associated with lengthier hospital stay and a five-fold higher frequency of death [10]. NMS patients have a seven-fold higher risk of losing >50 % of their blood volume during surgery compared to those without NMS, and curve progression might eventually reduce the patient's functional status to "fully dependent" [8, 31].

Pulmonary complications

Pulmonary complications are a prominent cause of morbidity and mortality in these high-risk patients [8, 32], with complication rates as high as 39 % [14].

In the current review, the overall PR is 22.71 % with 97.8 % variability. We observed a set of 6 studies (Fig. 1) reporting higher complication rates than the overall and remaining studies, but in a recheck of the individual studies we observed that these studies investigate severe CP and Duchenne's muscular dystrophy (DMD) (investigated by Marsh et al.). These two etiologies have an established high risk of pulmonary complications secondary to their disease pathology [10, 33, 34], which is also reflected in complication rates from the diagnosis sensitivity analysis (Figure 1b, supplement). In addition, the main objective of these studies was to analyze pulmonary complications solely in association with detailed pulmonary function testing. We hypothesize that the high rates in these studies are due to the specific and pure diagnosis of the patients they investigated coupled with the clear objective of reporting pulmonary complications and risk factors alone.

We found 1.98 % pulmonary complications in a large database study from Davis Reamers et al., which lies in the lower spectrum of complication rates shown in Fig. 1. This varies significantly from rates in large sample (>100) studies in the middle of the spectrum [35, 36]. One likely explanation for low rate could be the use of standardized surgical protocols, post-surgical care and data documentation in the American study compared to, among others, Bentley and Szoke et al.'s single-center studies [35, 36]. On the contrary, single-center studies are more likely to have meticulous documentation of all major and minor complications and hence higher rates. It was not feasible to segregate major and minor complications, as some authors report major complications and

some report the overall number of complications. Therefore, we suggest that these variations in rates are attributable to the studies' diverse methodologies and sample populations.

Few studies in the higher spectrum of complication rates cite age >16 years at the time of surgery as a prominent risk factor for prolonged mechanical ventilation [30, 37]. While such a specific pulmonary complication and age relationship cannot be analyzed by means of our sensitivity analysis, our analysis suggests no significant difference between complication rates and overall PR with respect to age at surgery. Moreover, rates with different sample sizes did not differ from the PR; hence, other methodological characteristics in combination could likely explain the wide heterogeneity.

The medical history of seizures in NMS patients has a positive association with higher pulmonary complications [33, 38]. Mohamad et al. [33] found that 22 out of 45 pulmonary complications occurred in patients taking seizure medication. Most of the studies in our review do not investigate this relationship in detail. We assume that the observed rates of pulmonary complications are influenced by the fact that NMS patients typically take antiepileptic medications.

High postoperative pulmonary complications of 31.08 and 46.6 % have been reported [16, 39] previously. Lung infiltrations and pneumothorax following a transthoracic approach contribute to these high complication rates [17, 39, 46]. All included studies report complications in a well-defined NMS population treated with a diverse surgical procedures (anterior, posterior spinal fusion, anterior and posterior combined approach). A majority of these studies do not stratify the complication rates based on the surgical procedure performed. Only Hod-Feins et al. [17] performed a surgical procedure subgroup analysis for complication rates and found that combined fusions correlated with higher pulmonary complications and longer ICU hospitalization in comparison to posterior spinal fusion (5.54, 4.05 days, respectively) and that longer fusion correlated with shorter ICU hospitalization.

In-depth investigation from our review suggests that the choice of surgical protocol is determined by a variety of factors: the patient's preoperative health status, the surgeon's preferred surgical approach and instrumentation, and the caretakers' preferred functional goals, to name a few, and consequently, it is impractical to develop a uniform surgical protocol in NMS patients. Irrespective of protocol choice, the objective should be to produce the desired outcome with the fewest possible pulmonary complications, as they are a prominent cause of morbidity and mortality in these high-risk patients.

Neurological complications

The current review found an overall PR of 3.01 %, which is comparable to rates from other studies (2.7, 4.6 %) [33, 40]. However, 5 studies in the lower spectrum of Fig. 2 report higher rates compared to the overall PR. Of these, Sponseller [41], Greggi [42] and Accadbled et al. [43] report about four- to eight-fold higher rates compared to the overall PR. We interpret that these studies have poor result precision with very wide confidence intervals and thus they should not influence the interpretations of results in totality. Moreover, because they have a small sample size, generalization in relation to results is not advisable. Although Modi et al, Sponseller et al. and Bentley et al. report high prevalence, the complications are transitory and, in comparison to permanent neurological complications, not disturbing. Bentley et al. point to curve severity and immobility status to explain the high neurological complication rate in their study. Many natural history studies support the interdependence of curve severity and immobility status [20]. Functional levels in patients with a greater degree and progression of scoliosis (80 vs. 56 degrees and 4.4 vs. 3.0 degrees per year, respectively) deteriorate sharply, leading in turn to increased nursing needs [31, 44]. Both Bentley et al. and Mohamand et al. suggest that the use of spinal cord monitoring and assessment of pre-existing motor compromise lead to good neurological outcome [35].

In the lower spectrum of rates, only a handful of studies report no complications. We reviewed these to discover a logical explanation. To our surprise, we found that all of them deal with a limited number (20–22) of patients with such challenging cases as congenital scoliosis with dysraphism, severe CP and non-ambulatory DMD with no reported complications. It was evident that the surgeons here used technically advanced instrumentations like third generation CD instrumentation, Modified Luque-Galveston, and segmental pedicle screw instrumentation [45–48]. As the authors explain, these instrumentations provide better biomechanical advantage and stability resulting in fewer implant failures and other implant-related complications, which are a significant cause of neurological complications [7, 47, 49, 50].

Reames et al. and Qui et al. report rates within the confidence interval of overall PR. Reames et al. found 64 neurological complications in a sample of 4,657 NMS patients, with 49 (1.1 %) new neurological deficits and 19 (0.4 %) nerve and plexus injuries. New neurological deficits were seen with revision procedures. Qiu et al. [13] found that the use of combined procedures, Cobb angle >90°, hyperkyphosis and revision surgery were risk factors for neurological deficits.

Our sensitivity analysis suggests that high complication rates (15.1 %) are affiliated with lower age at surgery, studies with >100 sample size and publications from the late 1990s. From publication-year sensitivity analysis, we can deduce that advances in anesthesia care, intensive care facilities and surgical constructs over time are responsible for the low complications in recent studies (2002–2011). Neurological complication can present *de novo* as well as a sequel to infections, implant-related problems and revision, which may explain the higher rates in the large sample studies.

Infection

Development of infection is unfavorable to the final outcome of scoliosis surgery. We found an overall infection PR of 10.91 %. Six studies report prevalence rates higher than the overall and remaining studies; we investigated this subset to identify likely reasons for the high rates. Ramirez, Szoke, Benson, Wimmer and Tsirikos et al. worked with severely afflicted non-ambulatory CP and DMD patients having a mobility status with a proven high infection risk [36, 51]. The patients in Szoke's et al. study were severely medically compromised, with malnourishment, speech incapacity, muscle release surgery, and seizure disorders exacerbating their CP disorder. Benson et al. and others performed extensive surgeries on high-risk myelomeningocele and spastic CP patients and reported a high frequency of urinary tract infections (5.3 vs. 0.7 %) and surgical wound infections (1.3 vs. 0.3 %), respectively [10, 36, 52]. The high risk of infections in myelomeningocele patients is also supported by results of our sensitivity analysis, depicting an infection rate of 20.32 % in this subgroup. The authors suggest that major surgery poses a high risk of infections in NMS patients and the observed high rates are therefore not surprising. It is interesting to note that the authors recommend surgery in these high-risk patients and they defend this argument on the grounds of high rates of satisfaction and functional improvement reported by the patients and their caretakers.

Our studies also observed that prolonged preoperative hospitalization, extended surgery duration, high blood loss [53, 54], cognitive impairment, severity of deformity, use of allograft [11, 51, 55], urinary tract infection and [54, 56] and malnutrition [57–59] are some of the complexities affiliated with surgical treatment of NMS patients and are also proven risk factors for infections. Szoke et al. [36] elaborate that the infected cases in their series had spastic quadriplegia with severe mental retardation, seizures and speech inability; these patients had also received allogenic transfusion subsequent to high blood loss.

At the lower spectrum of complication rates, a couple of studies show convincingly low infection rates. We observed lower rates of infections when advanced surgical approach and instrumentation [60, 65] were used for smaller Cobb angles [61] in adequately nourished patients [62]. The trend of decreasing complication rates with an increase in publication year suggests that advances in surgical approach, instrumentation and patient care have yielded a positive impact. We believe that the low rate reported by Barsdorf et al. [14] suffers from limitations in the type of data analyzed; their reported rates are calculated on the basis of hospital admissions due to infections. It is doubtful that every infection is reported to the same institute for treatment, hence the lower rates.

Implant-related complications

NMS patients have problematic fusion outcomes at follow-up. We report an overall implant complication PR of 12.51 %. Nine studies distinctly report much higher rates for implant complications compared to the overall. Accadbled et al. [42], Milbrandt and Johnston Ii [63], Greggi et al. [43] report imprecise results with very wide confidence intervals. We investigated the individual studies to discern plausible explanations for the observed results. Nectoux et al. [64] suggest that their spastic and non-ambulatory CP patients had increased risk of fractures with instrumented surgery. Phillips et al. [46] reported implant breakages with two types of spino-pelvic anchorages. They report 11 such complications with single screw stabilization compared to two screws. Two screws offer caudal stability, thus inhibiting the proximal motion that is responsible for stress failures of the implant. They prove that caudal stability diminishes implant complications. Comstock et al. [62] had greater than 5 years follow-up for 42 % of their patients, which explains the high implant complications when compared to studies which have a mean follow- up of approximately 2 years. On the other hand, Parsch et al. [65] attribute the high rates to the high level of paralysis seen in their myelomeningocele patients. They report that the higher the level of paralysis, the higher was the implant failure rate and correction loss. Again, Modi et al. [66, 67] and Comstock et al. [62] make interesting recommendations for surgery, which they argue on the basis of the patients' improved function and parents' satisfaction with the surgical results.

In the lower spectrum of complication rates, few studies report no complications. They are very diverse in objectives and surgical methods. As we were unable to isolate any common study characteristics which could explain the lower rates observed, we believe they are most likely a product of chance. Our sensitivity analysis suggests that a larger cohort exhibits lower implant complication rates (6.5 %). Sponseller et al. [56], whose main objective was to study infection rates after surgery, mention two cases of implant removal due to infection. Since their main objective was to report infections, other non-infection related implant complications, even if present, were not likely to be mentioned. Miladi et al. [68] and Tsirikos et al. [69] show low rates, consisting primarily of such minor complications as loosening and prominence with illiosacral and pedicle screws, respectively.

Pseudoarthrosis

Lack of bony fusion 1 year after surgery is classified as pseudoarthrosis or, in cases involving the spine, false joint formation [70]. Banit and coworkers [71] operationally define pseudoarthrosis as a "radiographic lucency or curve progression with hardware failure". We report a PR of 1.88 %. Strikingly high rates are seen in five studies, three of which have large confidence intervals and are therefore imprecise interpretations. Unlike other studies investigating multiple diagnoses, Banit et al. [71] and Geiger et al. [72] report high rates for myelomeningocele patients. Geiger et al. elaborate, that high pseudoarthrosis was associated with implant infection, loosening, fusion to sacrum, and high (48.7 %) correction loss. NMS patients' metabolism-related factors such as mal-absorption syndrome, phosphate depletion, vitamin D abnormalities, and anemia all have a detrimental effect on fusion rates [73].

In the 2000s, Banit et al. report a pseudoarthrosis rate of 16 % compared to 27–50 % in the late 1980s [74, 75], which presumably is attributable to improvements in surgical instrumentation and technique [71, 76]. Sponseller et al. [55] found an increased risk of pseudoarthrosis following deep spinal infection. Studies from, for example, Tsirikos et al. advise precautionary preventive measures and, if pseudoarthrosis develops, managing it by means of instrumentation replacement and bone grafting, whereas Phillips et al. discuss no influence of radiolucencies on the final clinical outcome [46, 77]. Because pseudoarthrosis in the included studies is radiologically confirmed, the reported rates are unlikely to exhibit disparity.

Conclusion

High rates of pulmonary, implant, and infection related morbidity rates were determined among surgically treated NMS patients. As expected, the PRs are affected by heterogeneity. Sensitivity analysis suggests that age at the time of surgery of <13 years is associated with high pulmonary, neurological, and pseudarthrosis complication rates. Large sample studies (>100) reported high rates of implant and neurological complications and studies in the late 1990s reported high pulmonary, infection and neurological complication. Myelomeningocele patients had high rates of infection, pseudoarthrosis and neurological complications. Therefore, age at time of surgery, sample size, publication year and diagnosis type partially explain the variability in PRs. The studies in the review present limitations with regard to relevant data variables (e.g. categorization of complications, diagnosis-based complication compilation) thus rendering further investigation impossible. We conclude that the meta-analysis presented provides a valuable compilation of information on the prevalence of surgical complication rates in NMS; it is imperative that these be considered and addressed by the surgeon during the decision-making process. The current level of evidence in published literature regarding surgical outcomes and complications with various surgical techniques in NMS ranges between 2+ and 2− and the subsequent recommendations are level C. We propose that these figures will assist the surgeon's knowledge of "what and how much to expect" when operating on these complex patients.

Conflict of interest None.

Appendix 1

See Table 4.

Table 4 Characteristics of included studies

Study identification number	Author	Publication year	Study design	Diagnosis	Sample size	Mean age (years)	Instrumentation type	Surgical approach
1	Sponseller et al.	1999	PC	Spina bifida	14	11–19	TSRH	Anterior only spinal fusion
3	Ramirez et al.	1997	RC	DMD	30	14.5	Luque–Galveston, CD and TSRH	Posterior segmental instrumentation
4	Reames et al.	2011	RC	NMS, MMD and others	4657	≤18	NA	NA
5	Nectoux et al.	2010	PC	Quadriplegic CP	28	16.4	Luque-Galveston	Posterior arthrodesis (one stage)
6	Sponseller et al.	2000	RC	NMS	210	14.1	Moss Miami, Cotrel-Dubousset, DePuy, Warsaw, Illiosacral screw	Posterior, anterior-posterior
11	Yazici Muharrem et al.	1997	RC	NMS	40	14.2	Galveston technique with isola instrumentation	Posterior fusion till pelvis
12	Miladi et al.	1997	RC	NMS	154	14.7	CD instrumentation, CD Galveston, Illiosacral screws	Posterior fusion till pelvis
13	Qiu et al.	2008	RC	NMS, IS	559	14	TSRH instrumentation. Moss Miami, CD, CDH Isola	Posterior, anterior-posterior, anterior
14	Cate et al.	2008	RC	NMS	46	13.5	NA	Posterior and anterior-posterior (1 stage)
15	Tsirikos et al.*	2003	RC	NMS	288	13.1	Unit rod instrumentation	Anterior-posterior
16	McCall et al.	2005	RC	NMS	55	13.5	Segmental pedicle screw instrumentation with U-rod	Posterior approach
18	Teli et al.	2005	RC	NMS	56	14	Luque-Galveston, 3rd generation	Posterior, anterior-posterior, anterior-posterior staged
19	Mohamen Hassen Mohamed Ali et al.	2010	RC	CP	236	13.8	Unit rod instrumentation	Posterior approach
21	Fazir Mohamad	2007	RC	NMS	175	14	NA	Anterior release and posterior fusion, anterior-posterior fusion, anterior instrumentation, posterior instrumentation
22	Banit et al.	2001	RC	Myelomeningiocele	50	12	Harrington's rod and segmental fixation	Posterior fusion
23	Kang et al.	2011	RC	NMS	74	17.3	NA	NA
24	Yuan et al.	2005	RC	NMS, IS and others	57	14	NA	NA
26	Gitelman et al.	2008	RC	NMS	12	15	Luque instrumentation with illaic screw	Posterior fusion
27	Benson et al.	1998	RC	NMS	50	13.6	Luque-Galveston, TSRH	Anterior-posterior fusion, posterior spinal fusion
28	Ko et al.	2007	RC	Myelomeningiocele	9	10.8	NA	Posterior fusion, anterior-posterior fusion

Table 4 continued

Study identification number	Author	Publication year	Study design	Diagnosis	Sample size	Mean age (years)	Instrumentation type	Surgical approach
29	Hod-Feins et al.	2007	RC	NMS, IS	31	14.3	Moss Miami, DePuy spine, Spine system evolution, TSRH	Posterior, anterior, anterior-posterior fusion
30	Master et al.	2011	RC	NMS	131	13.4	NA	Posterior segmental fusion, anterior-posterior fusion, pelvic fusion with Galveston
31	Thacker et al.	2002	RC	NMS	24	10.6	NA	Posterior, anterior-posterior, anterior
32	Sarwahi et al.	2001	RC	NMS	111	12.3	NA	anterior-posterior combined approach, staged approach, thoracolumbar approach
33	Modi et al.	2009	RC	NMS	50	18.1	Segmental instrumentation using pedicle screws	Posterior approach
34	Modi et al.*	2009	RC	CP	52	22	Pedicle screw fixation	Posterior approach
35	Modi et al.	2010	RC	NMS	27	14.7	Pedicle screw fixation	Posterior approach
36	Master et al.*	2011	RC	NMS	151	12.5	NA	NA
37	Tsirikos et al.*	2003	RC	NMS	45	15	Unit rod instrumentation with Galveston technique	Anterior-posterior combined, anterior-posterior staged
38	Piazzolla et al.	2011	RC	NMS	24	18.1	CD instrumentation	Anterior-posterior, posterior
40	Barsdorf et al.	2010	RC	NMS, IS	437	12.4	NA	NA
41	Phillips et al.	2007	RC	NMS	50	NA	Modified Luque-Galveston with pedicle screws	Posterior approach
42	Hahn et al.	2008	PC	DMD	20	14	Illiac screw pelvic fixation and Galveston technique	Posterior approach
43	Sponseller et al.	2010	RC	CP	157	13.5	Unit rod and custom bent rods	Posterior, Anterior-posterior (1 and 2 stage)
44	Smith et al.	2011	RC	NMS	5147	NA	NA	NA
45	Marsh et al.	2003	RC	DMD	30	14.8	Harrington's-Luque, AOUSS, Colorado and Synergie	Posterior approach
46	Teli et al.	2006	RC	CP	60	15	CD instrumentation	Posterior approach
47	Mehmet Ayvaz	2007	RC	Spinal dysraphism	22	12	Combination of hooks and pedicle screws	Posterior fusion with or without anterior release
49	Tsirikos et al.	2008	RC	NMS	287	13.9	Unit rod instrumentation	Posterior, anterior-posterior combined
50	Frischhut et al.	1997	RC	NMS	42	16.5	Luque, Luque-Galveston, CD and ISOLA	Posterior spinal fusion

Table 4 continued

Study identification number	Author	Publication year	Study design	Diagnosis	Sample size	Mean age (years)	Instrumentation type	Surgical approach
52	Szoke et al.	1998	RC	CP	172	13.9	Unit rod instrumentation	Posterior fusion with or without anterior release
53	Wimmer et al.	2005	RC	NMS	52	15.5	Luque and ISOLA instrumentation	NA
54	Peelle et al.	2006	RC	NMS	40	NA	Galveston technique with iliac screw	Anterior-posterior
55	Sengupta et al.	2002	RC	DMD	50	12.3	Luque pelvic fixation, Galveston lumbar fixation	NA
56	Arun et al.	2010	RC	DMD	43	12.9	Sublaminar, Pedicle screw and Hybrid	NA
58	Modi et al.	2008	PC	NMS	26	17.5	Pedicle screw fixation	Posterior approach
59	Bentley et al.	2001	RC	NMS	101	12.7	Modified Luque or Harrington's instrumentation with limited Moe's fusion	Posterior approach
60	Heller et al.	2001	PC	DMD	31	14.1	ISOLA system (pedicle screw, hooks, wires)	NA
61	Alman et al.	1999	RC	DMD	48	13	Luque sublamilar wires either with modified Unit rod or Galveston extension to pelvis	NA
62	Eagle et al.	2007	RC	DMD	100	14	NA	NA
63	Geiger et al.	1999	RC	Myelomeningiocele	77	12.8	Harrington's, Zielke amd CD instrumentation	Anterior release -posterior fusion and anterior instrumentation-posterior fusion
64	Accadbled et al.	2008	RC	Prader willi syndrome	16	12.3	CD, Luque, Harrington's, Moss Miami instrumentation	Anterior-posterior, posterior fusion
65	De Giorgi et al.	1999	RC	NMS, IS	17	15.8	3 Rod CD instrumentation	Anterior-posterior (staged)
66	Comstock et al.	1998	RC	CP	79	13.8	Luque and TSRH	Anterior-posterior (staged or combined
67	Aleissa et al.	2011	RC	NMS	63	14.3	NA	Anterior, posterior instrumentation and fusion, anterior-posterior
68	Cahill et al.	2010	RC	NMS	323	14.1	NA	NA
69	Stella et al.	1998	RC	Myelomeningiocele	29	12	NA	Anterior fusion instrumentation, posterior fusion instrumentaion and combined anterior and posterior
70	Muharrem Yazici	2000	PC	NMS	47	14.2	Isola-Galveston	Posterio fusion + instrumentation = 39. Posterio fusion + instrumentation +anterior desis = 8 (combination of staged *n* sequential procedures

Table 4 continued

Study identification number	Author	Publication year	Study design	Diagnosis	Sample size	Mean age (years)	Instrumentation type	Surgical approach
71	Greggi et al.	2010	PC	Prader willi syndrome	6	12.8	Hybrid instrumentation with sublamilar wires, hooks and screws	NA
72	Whitaker et al.	2000	RC	NMS	23	18.4	Isola, DePuy-acromed raynhams, MA	Posterior onstru + fusion with pedicle screws. Ant discectomy + fusion = 1. Sequential surgery = 3
73	Takaso et al.*	2010	PC	CP	20	13.1	Depuy Raynham, MA semental pedicle screw and rod construct	Posterior approach
74	Tsirikos et al.	2011	RC	CP	45	13.4	Pedicle screw rod construct	Post only, anterior and posterior combined
76	Parsch et al.	2001	RC	MMC	54	13.1	CD and Spine fix system	Posterior instrumentation and fusion, anterior fusion and posterior instrumentation, Anterior-Posterior fusion instrumentation
78	Rodgers et al.	1997	RC	Myelodysplasia	24	10.3	Pedicle screw fixation, with hooks, sublaminar wires or spinous process wires	Anterior-posterior approach
79	Takaso et al.	2010	PC	NMD	10	13	Segmental pedicle screw fixation	NA
80	Tokala et al.	2007	PC	NMS	9	14	Single rod USS, DePuy and Moss Miami	Posterior, anterior approach
81	Milbrandt et al.	2005	PC	DMD	7	11.6	Segmental spinal instrumentation	Posterior, interior approach
82	Gill et al.	2006	PC	Myopathy with respiratory failure	8	12	USS	Posterior approach

* Used to label large sample publications from same author and same year

PC Prospective cohort study, *RC* retrospective cohort study

Appendix 2

See Table 5.

Table 5 Characteristics of excluded studies

Study identification number	Title	Exclusion	Journal	Publication year	Author	Study design	Follow up (years)	Diagnosis	Sample size	Mean age (years)	Surgical approach
2	Bleeding and coagulation changes during spinal fusion surgery: a comparison of neuromuscular scoliosis and idiopathic scoliosis patients	Insufficient information	Paediatric critical care Medicine	2002	Kannan et al.	PC	NA	NMS, IS	25	13	Posterior, anterior, anterior-posterior (1, 2 stage)
7	Evaluation of high risk patients undergoing spinal surgery: a matched case series	Mean age is less than 4 years	Journal of Pediatric Orthopaedics	2010	Miller et al.	CS	NA	NMS	73	<4	Posterior, anterior-posterior
8	Factors predicting postoperative complications following spinal fusions in children with cerebral palsy	Insufficient data	Journal of Spine Disorders	1999	Lipton et al.	RC	NA	CP	107	14.3	Posterior spinal fusion
9	Fatal marrow emboli in a paediatric patient having posterior spinal instrumentation for scoliosis repair	Case report is excluded	Pediatric anaesthesia	2006	Joffe et al.	CR	NA	NMS	1	11	Posterior spinal instrumentation
10	Fatal pulmonary fat embolism following spinal fusion surgery	Case report is excluded	Pediatric critical care Medicine	2006	Stroud et al.	CR	NA	NMS	1	17	Anterior release and posterior fusion (2 stage)
20	Pediatric scoliosis surgery—The association between preoperative risk factors and postoperative complications with emphasis on cerebral palsy children	Sample repetition	Neuropediatrics	2007	Hod-Feins et al.	RC	NA	NMS, IS	21	15	Anterior, posterior and combined spinal fusion
17	Mycoplasma hominis deep wound infection after neuromuscular scoliosis surgery: the use of real-time polymerase chain reaction (PCR)	Case report is excluded	European Spine Journal	2006	Krijnen et al.	CR		NMS	1	11	Posterior approach
25	Rate of complications in scoliosis surgery: a systematic review of the Pub Med literature	Systematic review	Scoliosis	2008	Weiss et al.	Systematic review	NA	NMS	22 NMS studies	NA	NA
39	Delayed neurologic injury due to bone graft migration into the spinal canal following scoliosis surgery	Case report is excluded	Orthopedics	2003	Early et al.	CR	NA	NMS	1	9	Anterior-posterior (1 stage)

Table 5 continued

Study identification number	Title	Exclusion	Journal	Publication year	Author	Study design	Follow up (years)	Diagnosis	Sample size	Mean age (years)	Surgical approach
48	Spinal surgery in children with idiopathic scoliosis and neuromuscular scoliosis. What's the difference?	Weighed survey analysis and scores	Journal of Pediatric Orthopedics	2006	Murphy et al.	RC	NA	NMS, IS	1570	13.2	NA
51	Blood loss during posterior spinal fusion surgery in patients with neuromuscular disease: Is there an increased risk?	Insufficient data	Pediatric anaesthesia	2003	Edler et al.	RC	NA	NMS, others	163	14.2	Posterior approach
57	Selective anterior fusion and instrumentation for the treatment of neuromuscular scoliosis	Mean age is less than 10 years	Spine	2003	Basobas et al.	RC	2	NMS	21	10.2	Anterior fusion
83	Complications associated with thoracic pedicle screws in spinal deformity	Insufficient data	European Spine Journal	2010	Li et al.	RC	3.5	NMS, others	242	NA	Posterior approach
84	Minimizing complications with single submuscular growing rods: A review of technique and results on 88 patients with minimum two-year follow-up	Mean age is less than 7 years	Spine	2010	Farooq et al.	RC	2	NMS, others	88	NA	Posterior approach
85	Long term outcomes and complications of Luque unit rod instrumentation in surgical management of cerebral palsy and neuromuscular scoliosis	Retracted and full text not available	Journal of Bone and Joint Surgery (Br Ed)	NA	Howard et al.	NA	NA	NA	NA	NA	Insufficient
86	Pedicle screw-only constructs with lumbar or pelvic fixation for spinal stabilization in patients with Duchenne muscular dystrophy	Follow up duration is not clear	Journal of Spinal Disorders and Technique	2009	Mehta et al.	RC	3.1	DMD	36	NA	Posterior approach

PC Prospective cohort, *CS* case series, *RC* retrospective cohort, *CR* case report, *NA* not available

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