DOI: 10.1590/0100-69912014006004 Original Article

Nuss procedure for *Pectus excavatum* repair: critical appraisal of the evidence

Procedimento de Nuss para correção de Pectus excavatum*: avaliação crítica da evidência*

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A B S T R A C T

Objective: To evaluate the effectiveness and safety of correction of pectus excavatum by the Nuss technique based on the available scientific evidence. **Methods**: We conducted an evidence synthesis following systematic processes of search, selection, extraction and critical appraisal. Outcomes were classified by importance and had their quality assessed by the Grading of Recommendations Assessment, Development and Evaluation (GRADE). **Results**: The process of selection of items led to the inclusion of only one systematic review, which synthesized the results of nine observational studies comparing the Nuss and Ravitch procedures. The evidence found was rated as poor and very poor quality. The Nuss procedure has increased the incidence of hemothorax (RR = 5.15; 95% CI: 1.07; 24.89), pneumothorax (RR = 5.26; 95% CI: 1.55; 17.92) and the need for reintervention (RR = 4.88; 95% CI: 2.41; 9.88) when compared to the Ravitch. There was no statistical difference between the two procedures in outcomes: general complications, blood transfusion, hospital stay and time to ambulation. The Nuss operation was faster than the Ravitch (mean difference [MD] = -69.94 minutes, 95% CI: -139.04, -0.83). **Conclusion**: In the absence of well-designed prospective studies to clarify the evidence, especially in terms of aesthetics and quality of life, surgical indication should be individualized and the choice of the technique based on patient preference and experience of the team.

Key words: Funnel chest. Evidence-based medicine. Effectiveness. Surgical procedures, operative.

INTRODUCTION

Pectus excavatum, or funnel chest, represents about 90% of congenital chest wall deformities [1]. It is an anterior depression of the chest, symmetrical or not, combined with a dorsal deviation of the sternum and the third to the seventh ribs or costochondral cartilages [2]. the etiology is still unknown and recent study results remain inconsistent. The hypotheses on the pathogenesis are based on intrinsic factors (cartilage metabolism) and / or extrinsic ones (bone development disorder) [1,3].

The overall incidence of *pectus excavatum* (PE) is one to eight cases in one thousand individuals. In Brazil, there was a prevalence of 22% in the Midwest region [4] and 1.3% in children from the primary school system in the northern region [5]. This disease most often affects boys (9:1 ratio)[2,3], and usually it is not discovered early in life. Family history of chest deformity is present in one third of cases. Among the associated comorbidities, there is scoliosis, congenital heart disease and Marfan syndrome [3]. School children and infants usually display no symptoms. However, adolescent and adult patients may have reduced lung function and lower exercise tolerance [6]. In some instances, the aesthetic appearance involves psychosocial disorders requiring specific behavioral therapy[7].

The open surgical approach, initially proposed by Ravitch in the late 40s [6], represented the gold standard for the correction of PE till the beginning of the 90s. In 1998, Donald Nuss presented a minimally invasive technique as an alternative to open surgery, consisting of the retrosternal placing of a metal bar to correction of the anterior deformity [6]. Some modifications of the original technique have been developed since its initial description, including the use of thoracoscopy, development of special materials for dissection, stabilizers to prevent migration of the bar, peri-costal absorbable sutures and non-allergenic titanium bars [8].

Despite these advances, the indications for surgical repair of PE remain controversial. Most studies show improvement in lung function, exercise tolerance and postoperative cardiac output, while some authors have reported no benefit or decline in function, and suggest that the procedure is reserved only for aesthetic purposes [3].

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In this context, the aim of this study was to evaluate the effectiveness and safety of surgical repair of PE, specifically through the Nuss technique, based on scientific evidence available in the literature.

METHODS

Design

Evidence synthesis with systematic search and selection process, data extraction and critical appraisal.

Eligibility criteria

We considered eligible systematic reviews and meta-analysis of randomized controlled trials or cohort studies that compared the Nuss procedure to conventional methods of correction of the chest deformity in question. There was no restriction regarding language, country, date of publication, follow-up or sample size. The outcomes were: incidence of general complications, hemothorax, pneumothorax and reintervention.

Databases and search strategy

We held an electronic search in MEDLINE, Trip database, Cochrane Library and Center for Reviews and Dissemination (CRD).

The keywords were defined from the terminology arranged in the Medical Subject Headings (MeSH), using the following search strategy for MEDLINE (via PubMed): ("Funnel Chest" [MeSH] OR (Funnel Chests) OR (Pectus Excavatum)) AND "nuss" [tiab] AND systematic [sb]. This strategy was adapted for performing the search in the other databases.

Study selection and data extraction

Three researchers independently reviewed the titles and abstracts of the selected studies. The full text was obtained in cases where it was not possible to assess the eligibility through the summary. The same researchers checked all selected studies and any difference of opinion was decided after discussion and consensus. The selected studies were reviewed and those not related to the specific theme were excluded. Duplications were also removed.

We extracted the following variables: year, country, study design, population, sample size, intervention method, comparative method, postoperative complications, postoperative pain, need for further intervention, mortality, length of hospital stay, aesthetics and satisfaction of the patient.

Data analysis

We synthesized the extracted data for the construction of an evidence summary. All results were confirmed in previous studies for increased data reliability.

Association measures were relative risk (RR) and standardized mean difference with 95% confidence interval (95% CI). We recalculated the meta-analyzes for each outcome using the random effects model of Mantel Haenszel. Statistical heterogeneity of results was estimated by the I□ and chi-square tests (significance level of $p < 0.10$).

Bias risk assessment and quality of evidence

The risk of bias in the primary studies that comprised the evidence was assessed individually. For this evaluation, we used the Newcastle-Ottawa Scale [9], modified by the Brazilian Medical Association [10]. We evaluated the patient selection criteria (4 points), comparability (2 points) and measurement of outcome (3 points). Studies with a score greater or equal to six were considered of low bias risk.

We used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool to assess the quality of evidence available on selected and included studies[11]. This tool allows quality classification of the evidence on four levels: high, moderate, low and very low; outcomes from randomized clinical trials begin the assessment with high quality, and observational studies, with low quality. We classified outcomes as critical, important and unimportant and then we evaluated them for the study limitations, inaccuracy, inconsistency and publication bias. The quality level was reduced by one for each of the non-met factors. If the quality of the outcomes was not reduced, we would assess the factors that could increase the quality of the evidence.

RESULTS

The literature search located 51 articles. After removal of duplication and review of titles and abstracts, four reviews were selected. Of these, only one was included after assessment of the complete text in the light of the inclusion criteria (Figure 1).

The elected systematic review summarized the findings from nine cohort studies comparing minimally invasive Nuss technique and the conventional method of Ravitch published between 2001 and 2009[12]. In total they evaluated 1,081 patients, 671 who submitted to repair by the Nuss technique, and 410 treated by the Ravitch procedure.

Bias risk assessment and quality of evidence

The bias risk assessment showed that all studies had a low risk of bias [13-21] (Table 1). Studies have failed mainly on comparability between cases and controls and confirmation of the absence of the outcome at baseline. Important information, such as the degree of deformity of the chest wall, the learning curve and detailing on the expertise of the surgical team, were provided for better assessment of the similarities of the participants and exposure.

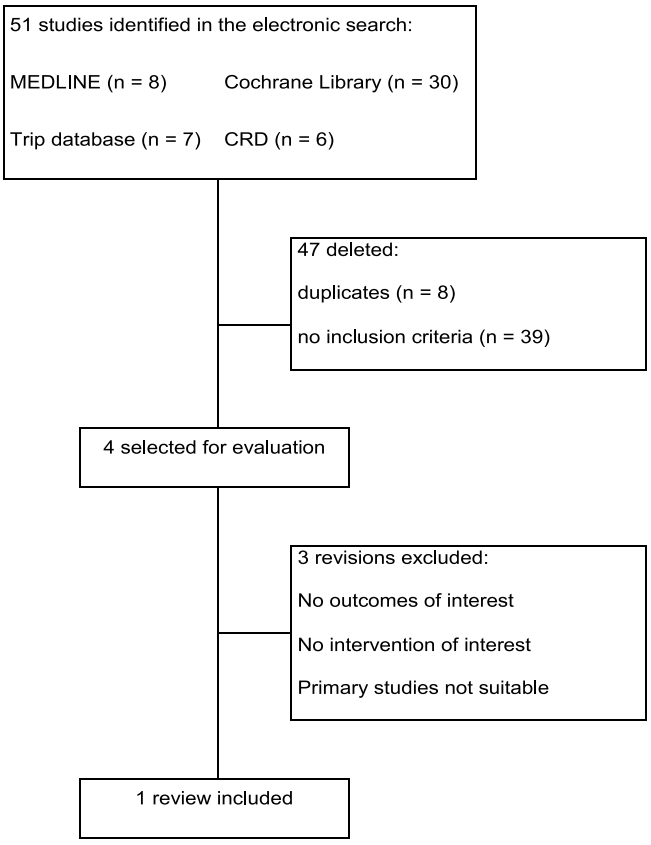

Figure 1 - *Selection and inclusion process of the studies in the review.*

The resulting evidence was classified as low and very low. The quality of outcomes was reduced from low (observational design) to very low, mainly due to inconsistency (mixed results) and imprecision (results not statistically significant) (Table 2).

Outcomes

The Nuss technique showed worse results in the following critical outcomes: incidence of hemothorax (RR = 5.15; 95% CI: 1.07-24.89; I^2 = 31%); pneumothorax (RR = 5.26; 95% CI: 1.55-17.92; I^2 = 65%); and need for reintervention due to migration of the bar or persistent deformity (RR = 4.88; 95% CI: 2.41-9.88; I^2 = 0%).

The Nuss procedure consumed less operating time compared with the Ravitch one (mean difference = -69.94 minutes, 95% CI: -139.04 to -0.83; I^2 = 99%), but the results were highly heterogeneous between studies.

There was no statistically significant difference between the procedures evaluated as for the following outcomes: general complications (critical), need for blood transfusion (important), time to ambulation (important) and hospital stay (important).

The use of different instruments to measure postoperative pain [13-20] and patient satisfaction [13,15,20] prevented these outcomes to be objectively evaluated.

Table 1 - Assessment of the bias risk of individual studies according to the Newcastle-Ottawa scale [9] adapted by the Brazilian Medical Association [10].

Study	Patient selection				Comparison	Outcome			Total
	Representativeness of the exposed	Selection of the exposed	Measurement of exposure	Absence of outcome	Similar groups	Outcome assessment	Appropriate follow-up	Complete follow-up	
Lam 2008[13]	1	1	1	0[b]	0[c]	1	1	1	06
Antonoff 2009[14]	1	1	1	1	0[c]	1	1	1	07
Miller 2001[15]	1	1	1	0[b]	0[c]	1	1	1	06
Inge 2003[16]	1	1	1	0[b]	0[c]	1	1	1	06
Kelly Jr 2008[17]	1	1	1	1	0[c]	1	1	1	07
Molik 2001[18]	1	1	1	0[b]	0[c]	1	1	1	06
Fonkalsru 2002[19]	1	0[a]	1	0[b]	0[c]	1	1	1	05
Jo 2003[20]	1	1	1	0[b]	0[c]	1	1	1	06
Boehm 2004[21]	1	1	1	0[b]	0[c]	1	1	1	06

[a] Not exposed from another hospital.
[b] Does not specify whether the outcomes are absent at the beginning of the study or if patients have previously been through the operative process.
[c] Basal Characteristics not evaluated statistically as for the similarity of the groups.

Table 2 - Evaluation of the quality of evidence and summary of results using the GRADE tool [11].

Outcomes	Evaluation of the quality of evidence[a]			N. of patients [events/total or N (AV ± SD)]		Effects		Quality	Importance
	N. of studies (references)	Inconsistency	Inaccuracy	Nuss	Ravitch	Measure of Association	Result (95% CI)		
General complications	9[13-21]	Very serious[b]	Serious[c]	225/671	63/410	Relative risk	1,56 (0,75; 3,24)	Very low	Critical
Hemothorax	4[15,18,20,21]	-	Serious[c]	7/123	3/243	Relative risk	5,15 (1,07; 24,89)	Very low	Critical
Pneumothorax	7[14,15,17-21]	Serious[c]	-	30/319	12/651	Relative risk	5,26 (1,55; 17,92)	Very low	Critical
Reintervention	7[14-16,18-21]	-	-	32/368	7/343	Relative risk	4,88 (2,41; 9,88)	Low	Critical
Blood transfusion	2[15,21]	-	Serious[c]	1/101	1/39	Relative risk	0,40 (0,04; 3,63)	Very low	Important
Time of hospitalization	4[13,14,19,20]	Very serious[b]	Serious[c]	208 (5,7 ± 0,95)	235 (6,1± 0,95)	Average difference	-0,4 dias	Very low	Important (-2,86; 2,05)
Duration of surgery	5[13,14,19,20,21]	Very serious[b]	-	229 (75,36± 24,61)	242 (145,34 ± 25,78)	Average difference	-69,94 min. (-139,04; -0,83)	Very low	Important
Time to ambulation	2[13,20]	Very serious[b]	-	126 (5,00 ± 1,00)	40 (7,7 ± 2,18)	Average difference	-2,7 dias (-10,25; 4,84)	Very low	Important

Notes:
All studies were observational and initiated the evaluation with low quality.
The presence of publication bias could not be evaluated due to the low number of studies.
The outcomes "patient satisfaction" and "postoperative pain" could not be summarized because they were measured by different methods between studies.
Such outcomes have not lost points in any of the evaluated criteria and remained with low evidence.
[(a)] The items "limitations" and "indirect evidence" did not show serious flaws in any outcome.
[(b)] High Heterogeneity (I^2 test above 75% and Chi-square test with p-value < 0.10).
[(c)] Inaccurate confidence interval.
[(d)] Moderate Heterogeneity (I^2 test between 30-75% and Chi-square test with p-value < 0.10).
Abbreviations:
95% CI – 95%confidence interval.
N. – number.
AV – average.
SD – standard deviation.
min-minutes.

DISCUSSION

This evidence summary rekindles the debate on the effectiveness and safety of the main surgical techniques for correction of *Pectus Excavatum* in light of the critical evaluation of methods of clinical evidence available in the literature.

Despite the lack of significant differences between the Nuss and Ravitch techniques regarding the general postoperative complications, the current evidence relates with higher risk of incidence of critical outcomes, such as hemothorax, pneumothorax, and need for surgical intervention [22]. The Nuss technique was superior to the Ravitch technique when as for the duration of the operation.

We classified the quality of the evidence in question as very low. It is possible that future studies change these estimates significantly, especially regarding the short term effects of the Nuss technique [11]. There is a systematic review protocol registered in the Cochrane Database of Systematic Reviews, but without results published so far [23].

The aesthetic aspect remains a major indication for repair [1]. However, this parameter is superficially evaluated by the available literature [12,24]. The validation of instruments to evaluate this outcome is necessary to increase the understanding of the processes involving the psychosocial aspects of the deformity, especially in patients of different age groups and cultural characteristics [24].

Despite the anesthetic and pain control strategies have been poorly explored in this population [25], many surgeons, based on everyday experience, report greater discomfort in patients undergoing the Nuss technique. Furthermore, the impact of pain management on patient satisfaction was not yet systematically evaluated [1,16].

In a retrospective cohort developed in the United States, there was an increase of 12% in direct costs in the Nuss group, but the total hospitalization costs were lower, with a saving of 27% in patients undergoing the minimally invasive technique [16,24]. Complete economic evaluations on this technology, however, are not available [1,12].

In an attempt to standardize the surgical indications, criteria have been proposed for repair of PE based on the severity of symptoms and anatomical deformity, CT and ultrasound profile, and prior surgical repair failure [6].

The Nuss method is preferably used in children and adolescents [26,27]. The results generally tend to be less favorable in adult patients, in which the chest is less flexible, making them more susceptible to complications and postoperative pain [26]. Conversely, a retrospective analysis of 52 patients older than 30 years demonstrated similar clinical results to those of adolescents and children, despite the increase in surgery time and the number of metal bars used in the procedure [28]. Recently, innovative approaches [29] involving vacuum treatment and the use of a magnetic implant for replacement of the sternum have been reported and are in phase 1 of their clinical trials [1].

Comparisons between techniques require well-designed and well-conducted, multicenter studies, with methodological quality higher than the ones of the currently available observational studies [3,30]. The increase in the number of patients around the world, combined with a long follow-up period, will allow clarification of the age limits, more precise surgical indications, time to remove the metal bar, and accurate assessment of aesthetics and quality life [3,8].

In conclusion, well-designed prospective studies are needed to clarify the evidence in the area, especially on the aesthetics and quality of postoperative life. In this context, the indication for the procedure should be individualized, and the choice of technique, based on preference and experience of the surgical team and the institution.

Acknowledgements

The authors thank the researchers Andrea Costa de Andrade (HUGV / UFAM) for assistance in the studies selection, and Waneska Andressa Martins da Silva Caldeira and Cyro Barbosa (UNB) for their help in reviewing the manuscript.

RESUMO

Objetivo*: avaliar a efetividade e segurança da correção de* pectus excavatum*, através da técnica de Nuss, com base nas evidências científicas disponíveis.* ***Métodos****: realizou-se uma síntese de evidências seguindo processos sistemáticos de busca, seleção, extração e avaliação crítica. Os desfechos foram classificados pela importância e tiveram sua qualidade avaliada pela ferramenta* Grading of Recommendations Assessment, Development and Evaluation *(GRADE).* ***Resultados****: O processo de seleção dos artigos culminou na inclusão de apenas uma revisão sistemática, a qual sintetizou os resultados de nove estudos observacionais comparando o procedimento de Nuss e ao de Ravitch. A evidência encontrada foi classificada como baixa e muito baixa qualidade. O procedimento de Nuss causou maior incidência de hemotórax (RR=5,15; IC95%: 1,07; 24,89), pneumotórax (RR=5,26; IC95%: 1,55; 17,92) e necessidade de reintervenção operatória (RR=4,88; IC95%: 2,41; 9,88) quando comparado ao de Ravitch. Não houve diferença estatística entre os dois procedimentos nos desfechos: complicações gerais, transfusão de sangue, tempo de hospitalização e tempo para deambulação. A operação de Nuss foi mais rápida que a de Ravitch (diferença média [MD] = -69,94 minutos; IC95%: -139,04, -0,83).* ***Conclusão****: Na ausência de estudos prospectivos bem delineados para clarificar a evidência, sobretudo quanto à estética e à qualidade de vida, a indicação operatória deve ser individualizada e a escolha da técnica baseada na preferência do paciente e experiência da equipe.*

Descritores: *Tórax em funil. Medicina baseada em evidências. Efetividade. Procedimentos cirúrgicos operatórios.*

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Received 20/11/2013
Accepted for publication 28/02/2014
Conflict of interest: none.
Source of funding: none.

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