An Open, Prospective Study to Evaluate the Effectiveness and Safety of Hyaluronic Acid for Pectus Excavatum Treatment

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Abstract

Background: Pectus excavatum (PE) is sometimes associated with psychological and physiological difficulties influencing a patient’s quality of life. Treatment with a hyaluronic acid (HA)-based gel may benefit patients and be an alternative to other more invasive treatments.

Objectives: The authors sought to evaluate the effectiveness in terms of satisfaction, duration, and safety of HA gel treatment for PE including impact on quality of life.

Methods: Males ≥18 years having PE without functional problems received HA gel injections (50 – 150 mL) at the site of deformity and in some cases at the medial pectoralis muscle borders to optimize the aesthetic result. Follow-up visits were performed after 1, 3, 6, 12, and 24 months with optional retreatment at the 24-month visit including a 1-month follow-up. Evaluations included Pectus Excavatum Evaluation Questionnaire, patient satisfaction, magnetic resonance imaging, and safety assessments.

Results: The treatment significantly improved patients’ self-esteem ($P < 0.001$) and psychosocial function ($P \leq 0.038$) throughout the study, as assessed by Pectus Excavatum Evaluation Questionnaire. Patients were satisfied with the aesthetic outcome and considered the treatment mild in terms of level of pain during injection. Treatment effects were maintained up to 24 months and 58% of the HA gel remained at this visit, shown by Magnetic Resonance Imaging measurements. The treatment was well tolerated.

Conclusions: Treatment of PE with HA gel improved patient quality of life related to self-esteem and psychosocial functioning including aesthetically pleasing results. The treatment may also offer benefits in terms of safety and tolerability compared with other treatments.

Level of Evidence: 4

Pectus excavatum (PE) is a congenital chest-wall deformity affecting about 1 in 800 individuals.¹ The deformity results in a caved-in appearance of the chest and is commonly associated with psychological problems including social withdrawal and feelings of anxiety or depression.² The psychological effects are not necessarily dependent on the PE severity,³,⁴ but severe deformities may impair cardiac and respiratory function and cause pain.⁵ Although these functional problems are important indications for surgery, many patients seek treatment primarily for cosmetic or psychological reasons.⁶,⁷

Surgical treatments for PE include the invasive Ravitch procedure⁹ and the minimally invasive Nuss procedure (minimally invasive repair of pectus excavatum).¹⁰ The...
Nuss procedure has been associated with complications such as bar placement and pneumothorax, and the hospitalization time after bar insertion is between 3 and 12 days. In addition, solid silicone implants have been utilized for many years with the benefit of offering shorter postprocedural downtime compared with the Nuss procedure. Aesthetic outcomes and patient satisfaction are positive in most cases; however, complications are common and visibility of implant, especially in patients with little subcutaneous fat, has been described.

Nonsurgical treatment options for mild PE include the use of a vacuum bell that is applied to the chest daily, elevating the chest wall over several months to years. The procedure is most likely to benefit younger patients or patients with mild PE and is not associated with serious complications. The use of the permanent dermal filler Bio-Alcamid (polymeric polyalkylimide) has been reported in a few publications, although the nonreversibility and difficulties in handling adverse events (AEs) have limited its use. The nonreversibility and difficulties in handling adverse events (AEs) have limited its use.

Macrolane VRF 20 (hereafter referred to as hyaluronic acid [HA] gel [Galderma, Uppsala, Sweden]) is a biodegradable HA-based filler produced with non-animal stabilized HA technology. The HA gel has a well-documented safety profile and has been investigated for volume and contour enhancement of the breasts and buttocks, making it an interesting alternative in terms of PE restoration. Indeed, Sinna and colleagues have reported encouraging results of a PE treatment case employing HA gel where the patient quickly returned to normal life without major complications. Note that the HA gel product was, as of November 2016, discontinued.

Because PE is associated with psychological problems and surgical treatments have long recovery times or lack documentation, a treatment alternative using the highly biocompatible HA gel was thought to be valuable for PE patients without functional impairments. Thus, the purpose of the study was to evaluate treatment with HA gel for PE in terms of effectiveness, duration, safety, and quality of life.

METHODS
Study Design
This was an open, noncomparative, 24-month study performed at one center in Sweden and one in France. Males (≥18 years) having PE without functional problems, defined as score 4 (“never”) on Pectus Excavatum Evaluation Questionnaire (PEEQ) questions 10 through 12 (Table 1), and with normal cardiac and pulmonary function were eligible. Exclusion criteria included previous PE treatments; presence of any bleeding or immune system disorder, including severe allergies; or hypersensitivity to anesthetics or HA. The protocol was approved by local ethics committees (Regional Ethical Review Board in Stockholm, Sweden and North-West II Ethics Committee in Amiens, France) and aligned with good clinical practice guidelines and the Declaration of Helsinki. All patients provided informed consent.

Patients received treatment at baseline, and an optional touch-up was performed after 6 to 7 weeks to obtain optimal results. Patients were followed for 24 months. An optional re-treatment was offered at the 24-month visit.

The first patient entered the study December 2012 and the last patient completed the study September 2016.

Treatment
All patients received local anesthetics and antibiotics before treatment. The volume of HA gel injected was assessed on an individual basis considering the goal to obtain an optimal correction of the PE deformity for the individual patient. A volume of 50 to 150 mL HA gel was recommended to provide adequate correction of the deformity. There were no described variations in injection technique based on location of the deformity other than that the injection site was selected to facilitate the placement of the injected material. Briefly, incisions of between 1 and 2 mm (using a no 11 scalp blade) were made close to the deformity site with the patient in supine position. The product was injected in small quantities in the deep subcutaneous plane close to the bone while applying light pressure and gently withdrawing the 12-G or 16-G cannula. Touch-up after 6 to 7 weeks was given if needed for optimal correction utilizing a recommended volume of ≤20 mL HA gel. The re-treatment volume, if given at 24 months, could not exceed the volume administered at baseline.

Physical Examinations
General physical examinations were performed at screening and at the 24-month visit. Any functional defects due to the PE were evaluated by electrocardiogram, echocardiogram, and pulmonary function assessments. Complementary chest X-ray and Magnetic Resonance Imaging (MRI) examinations were performed at screening on all patients. Screening MRI examinations were done to obtain baseline Haller index scores for PE deformity severity assessments.

Assessments
Pectus Excavatum Evaluation Questionnaire
Patients’ quality of life regarding general self-esteem, psychosocial function, and physical function were assessed at screening and at each follow-up on the PEEQ. The PEEQ employed was adapted with parts from both the original
Patient Satisfaction

Patient satisfaction questionnaires were collected at each visit except screening and touch-up. Questions on patients’ opinion and pain regarding the treatment procedure were asked after baseline and re-treatment, and questions about satisfaction were asked at all follow-up visits. See Table 2 for details.

Magnetic Resonance Imaging

Patients were examined by MRI at 1 and 12 months after baseline to assess placement and volume of remaining product compared with baseline. Additional MRI was carried out on Swedish patients 24 months after baseline and at the re-treatment follow-up visit, with comparisons to the 24-month visit.

Table 1. Pectus Excavatum Evaluation Questionnaire

| Component                  | Question                                                                 |
|---------------------------|--------------------------------------------------------------------------|
| 1. General self-esteem    | How do you feel about:                                                   |
|                           | 1. The way you look in general?                                           |
|                           | 2. The way you look without your shirt or top on?                         |
|                           | 3. Having to spend the rest of your life as your chest looks now?          |
|                           | How often:                                                               |
|                           | 4. Do other people make fun of you because of your chest?                 |
|                           | 5. Do you avoid doing things like spending the night at friend’s house, going exercising or swimming, because of the way your chest looks? |
|                           | 6. Do you try to hide your chest to keep people from looking at it?       |
|                           | 7. Are you bothered because of the way your chest looks?                  |
|                           | 8. Does your chest make you feel shy or self-conscious?                    |
|                           | 9. Do you feel bad about yourself because of the way your chest looks?    |
| 2. Physical function      | How often has your chest caused you:                                     |
|                           | 10. Problems with chest pain while exercising?                            |
|                           | 11. Shortness of breath?                                                 |
|                           | 12. To feel tired?                                                       |
| 3. Psychosocial function  | How often has your chest caused you to feel:                             |
|                           | 13. Irritable?                                                           |
|                           | 14. Frustrated?                                                          |
|                           | 15. Sad or depressed?                                                    |
|                           | 16. Restless?                                                            |

Questionnaire adapted from: Lawson et al.28 and Krasopolous et al.12 Scoring questions 1-3: very dissatisfied = 1, mostly dissatisfied = 2, mostly satisfied = 3, very satisfied = 4; questions 4-16: very often = 1, often = 2, sometimes = 3, never = 4.

PEEQ by Lawson and colleagues28 and from a modified PEEQ by Krasopolous and colleagues (Table 1).12

Table 2. Patient Satisfaction Questionnaire

| Question                                                                 | Scoring                   |
|--------------------------------------------------------------------------|---------------------------|
| Patient assessment of treatmenta                                         | 0. Very unpleasant        |
| 1. Which of the following alternatives corresponds best with your opinion of the treatment procedure? |
| Pain during treatmenta                                                   | 0. Unbearable pain         |
| 2. Please assess the level of pain you experienced during the injectable treatment. |
| Satisfactionb                                                           | 0. A lot worse             |
| 3. How would you describe that the treatment has changed how your chest looks? |
| 4. How has the treatment changed how your chest looks?                   | 0. Much better            |
| 5. How has the treatment changed your opinion of your looks in general?  | 1. Severe pain             |
| 6. How satisfied are you that you performed the treatment?              | 2. Moderate pain           |

*Baseline and 24-month visits only. **All follow-up visits.

Health-Related Quality of Life

Patients’ Health Related Quality of Life (HRQoL) was an exploratory endpoint, assessing patients’ emotional and physical state and its impact on daily life and activities using the 12-item, short-form health survey version 2 (SF-12v2, referred to as SF-12)29 and the EuroQol 5-dimension 3-level (EQ-5D-3L) questionnaire.30 The EQ-5D-3L also included a current health status test ranging from 0 to 100 (worst to best imaginable health state). Answers to both questionnaires were collected at baseline and after 6, 12, and 24 months.

Productivity and Social Life

Productivity and social life were an exploratory endpoint and assessed patients’ ability and productivity regarding work and normal activities. Difficulties in social life, social engagement, and relationships in relation to the look of the chest were also assessed. Questionnaires were collected at baseline and after 1, 3, 6, 12, and 24 months.

Safety

Post-treatment expected events were collected via patient diaries between day(s) 0 through 13. Symptoms included bruising, itching, pain, redness, soreness, and swelling. Symptom presence and intensity (mild, moderate, or severe) was recorded; any event present at day 14 was to be reported as an AE. In addition, patients’ downtime (time away from work or school) and any time spent in hospital were collected. Investigators performed regular deformity examinations to assess presence of any abnormalities, capsular contractions, implant dislocation, asymmetries, or nodules.
Statistics

The safety and intention-to-treat populations were equivalent and defined as all HA gel-treated patients; analyses were performed using the intention-to-treat population. Re-treatment results are from the Swedish site patients. Changes in mean PEEQ component scores, that is, general self-esteem, questions 1 to 9; physical function, questions 10 to 12; and psychosocial function, questions 13 to 16, were assessed by means of Wilcoxon signed-rank tests. Other endpoints were summarized and presented descriptively.

RESULTS

Demographics and Baseline Characteristics

A total of 32 male patients were screened and 23 of those were included. Mean age was 41 years (range, 20-64 years) and average weight was 79 kg (range, 64-99 kg) and height was 183 cm (range, 163-203 cm). All had normal body mass index, blood pressure, and a PE defect without functional impairment according to PEEQ items 10 through 12 and screening examinations. Eleven (48%) patients had asymmetric PE deformities, and the left rib-cage side was the highest side in all patients. Mean Haller index scores inhaling and exhaling were 3.6 (range, 2.4-6.5) and 4.5 (range, 2.7-9.5), respectively. One patient was lost to follow-up after the 6-month visit and one was lost prior to the re-treatment follow-up.

Treatment

The mean volume of HA gel injected at baseline was 149 mL (range, 80-245 mL). Eight (35%) patients received touch-up, where an additional 22.5 mL (range, 20-40 mL) HA gel was administered on average. Total mean volume injected at baseline and touch-up was 157 mL (range, 80-245 mL). Mean injection time at baseline and touch-up was 21 minutes (range, 5-45 minutes) and 10 minutes (range, 8-10 minutes), respectively. Investigators performed actions to maintain a natural sternum depression (eg, placing a roll of gauze) in about half of the baseline treatments and in 13% of the touch-up treatments. Six (26%) patients (5 from the Swedish site presented here) where offered and received re-treatment, receiving 124 mL (range, 60-180 mL) HA gel on average, yielding a total study volume of 294 mL (range, 140-425 mL) in re-treated subjects. Reasons for not consenting to re-treatment included personal reasons (n = 4); no need for re-treatment (n = 2); central accumulation (n = 1); treatment effect too short (n = 1); and treatment too complicated (n = 1). Efficacy evaluations performed after re-treatment are not presented due to the low number of patients (n = 4) at the follow-up visit.

Effectiveness

Pectus Excavatum Evaluation Questionnaire

Patients’ mean PEEQ scores regarding general self-esteem and psychosocial function, but not physical function, were significantly increased at each visit compared with baseline (Figure 1). Thirty-nine (39%) patients reported being satisfied (very or mostly) at baseline with how they looked without a shirt and 44% with spending the rest of their life as their chest looked now. These proportions increased to 91% for both parameters after treatment and remained increased throughout the 24-month visit where 82% and 77% of patients, respectively, reported being satisfied. In addition, around 80% of patients reported hiding their chest, being bothered or feeling shy or self-conscious because how their chest looked before treatment. After treatment, these proportions had decreased to approximately 50%. On questions pertaining to psychosocial function, up to 35% of patients reported feeling irritable, frustrated, sad or depressed, and restless in the month preceding treatment. At month(s) 1 and 24, at most 13% and 5%, respectively, reported any of these
feelings in the preceding month. Details are presented in Figure 2 and Supplemental Table 1. See Figures 3 and 4 for photographs of a representative patient.

**Patient Satisfaction**

The questionnaires were marked with a unique patient number that could be traced to the patient only through
a patient identification log kept at the study site. All patients agreed that both the baseline injection treatment and the re-treatment was acceptable. In line with this, 87% of patients experienced no or only mild pain at the baseline treatment; no patient reported any pain at the re-treatment.

All patients agreed that the chest looked better (much or a little) up to 6 months after treatment and 76% of patients still thought the chest looked better at the 24-month visit. All re-treated patients agreed that their chest looked better at the re-treatment follow-up. When patients were asked about whether their feelings of how their chest looked had changed after treatment, ≥85% answered much or a little better at all follow-up visits. Moreover, ≥90% of patients agreed that their looks in general were improved up to the 12-month visit. At 24 months after treatment, 72% considered their looks in general as improved and at the re-treatment follow-up, 75% answered improved. See Supplemental Table 2 for details.

**Magnetic Resonance Imaging**
Product-placement assessments by MRI showed that the product was located as intended. Volume assessment showed that 67% (range, 35%-99%) of product remained after 12 months and 58% (range, 23%-85%) after 24 months. See Figure 5 for representative MRI patient

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**Figure 3.** Long-term treatment effect as shown by this representative 48-year-old male patient with pectus excavatum without functional problems. The patient was administered 154 mL hyaluronic acid gel to obliterate the pectus but also to strengthen the medial pectoral muscle border. (A) Before treatment, (B) 3 months post-treatment, (C) 1 year post-treatment, and (D) 2 years post-treatment.
images. The patients that had re-treatment at 24 months including an MRI 1 month after re-treatment (n = 4) had 85% of study product remaining from the 260 mL injected at baseline, touch-up, and re-treatment.

Health-Related Quality of Life
The HRQoL assessments in terms of SF-12 and EQ-5D-3L showed only minor changes after treatment. The vast majority of patients reported very good or excellent health without pain/discomfort or anxiety/depression; mean EQ-5D-3L current health-status score was 88 at baseline and 89 after 24 months. No limitations in activities or accomplishments due to patients’ physical or mental status were reported (data not shown).
Figure 4. Treatment effect as shown by this representative 25-year-old male patient with pectus excavatum without functional problems. The patient was administered 80 mL hyaluronic acid gel. (A, E) Before treatment, (B, F) 1 month post-treatment, (C, G) 3 months post-treatment, and (D, H) 6 months post-treatment.
event was soreness, reported by all patients. Three events were ongoing at day 14 and were reported as AEs. Mean downtime was 1.4 days (range, 1-3 days); an average 11 days (range, 1-21 days) was required to resume normal activities. A small number of abnormalities, capsular contractions, implant dislocation, asymmetries, and nodules were identified by palpation at the follow-up visits and were reported as AEs.

There were 72 AEs reported by 22 (96%) patients. Of these, 39 events by 19 (83%) patients were assessed as related to the product or injection procedure. Most related AEs (87%) were mild in intensity. The median duration of the related AEs was 64 days and 5 events (implant site reaction) in 3 patients were ongoing at study end, all mild in intensity. The most commonly reported AE was

**Figure 5.** Magnetic resonance imaging pictures showing remaining product after 1, 12, and 24 months from the same representative patient as in Figure 4 (a 25-year-old man). Volume estimates for this patient were 48 mL at month 1, 38 mL at month 12, and 31 mL at month 24. Investigators assessed that the product was located as intended at all visits. (A) One month after treatment, (B) 1 year after treatment, and (C) 2 years after treatment.
implant-site nodules; 8 patients (35%) reported 8 events; all were mild in intensity and recovered after a median duration of 183 days. Capsular contraction occurred as 8 events in 7 (30%) patients; all were mild in intensity and had a median duration of 169 days. AE details are presented in Table 3.

### DISCUSSION

This was an open, 24-month study evaluating the use of HA gel for treatment of PE in patients without functional problems. Treatment efficacy assessments were chosen to focus on improvement in self-esteem and emotion because this is the most common reason for PE patients to seek help with their condition. Effectiveness evaluations included assessments of patient satisfaction, quality of life, and study product placement and duration. The safety aspects of the treatment were evaluated in terms of physical examinations, expected post-treatment events, and AEs, as well as recovery time including factors such as sick leave and hospitalization.

An average volume of 157 mL (range, 80-245 mL) of HA gel was injected in total at baseline and touch-up; this injection volume is somewhat larger than what has been reported for similar procedures. A volume of 50 to 150 mL HA gel was estimated as sufficient and recommended to provide correction of the deformity. Estimating the filler volume required is, however, difficult due to the irregularity of the defect, and therefore a step-wise approach of filler administration over different appointments is common. In the current study, injection was performed at one occasion with optional touch-up after 2 weeks, which alongside differences in PE severity or investigator-assessed volume requirement can explain the rather high injection volume. Because the aim was to achieve aesthetically agreeable correction of the deformity for each patient, and because the size and shape of the...
deformity will vary in each patient, a different volume of filler was likely to be required for each patient. It was therefore decided not to limit the amount of injected material but to provide recommendations. The amount of unreacted cross-linker, 1,4 butanediol-diglycidyl-ether, which has mutagenic potential, is held at trace amount in dermal fillers. According to the Macrolane Instructions for Use, no more than 600 mL gel should be injected at one time, that is, many times higher the amounts injected in this study. Nevertheless, the amounts within the study are larger than those reported from similar procedures that were the basis for the recommended dose in this study. The comparably high dose needed to reach optimal reconstruction is explained by the PE severity.

Results showed that patients’ quality of life was improved, as evident by the significantly increased mean value in PEEQ general self-esteem and psychosocial function. When asked at baseline, patients were particularly concerned about the look of their chest; around 80% of patients reported being bothered or feeling shy because of the look of the chest, while over 90% reported satisfaction with their looks in general. Notably, despite the fact that PEEQ satisfaction with looks in general was very high both before and after treatment, almost all patients reported in the patient satisfaction questionnaires that the treatment had improved their opinion on their looks in general. The improvements in PEEQ items relating to the look of the chest are encouraging because many PE patients have negative evaluations of their body, leading to lowered quality of life. These data on PEEQ improvements are in line with previous studies using more invasive procedures, indicating that less-invasive interventions may be sufficient for certain PE patients.

Patient satisfaction assessments corroborated the improvement in the PEEQ as patients generally regarded their looks in general, look of chest, and feelings about look of chest as better compared with pretreatment. The proportion of satisfied patients decreased over time; however, still at the 24-month visit, at least 71% of patients regarded these items as improved.

MRI showed that 67% of the HA gel remained 12 months after treatment and 58% after 24 months. Assuming that patient satisfaction on looks in general, look of chest, and feelings about look of chest depend on the PE-deformity correction, the decline in satisfaction up to the 24-month visit can at least partly be explained by product degradation. Other studies including data on HA-gel degradation have shown slightly faster degradation; in one study evaluating the HA gel for breast enhancement, 34% of product remained after 12 months and 19% after 24 months (data on file). The follow-up to that study showed similar results. When the HA gel was used for buttock augmentation, 36% remained after 12 months and 24% after 24 months. The discrepancy between the rate of product degradation between those studies and present results may be due to body compartment differences in local blood flow and amount of hyaluronidases present. Another possible explanation could be the minimal movements in the treatment area.

The HRQoL assessments and the productivity and social life questionnaire were exploratory study endpoints, and the treatment had little effect on these endpoints. This is most likely because this was a relatively healthy sample of patients with no baseline functional impairments.

The treatment was well tolerated; the overall incidence of AEs was comparable to a previous study utilizing the HA gel for breast augmentation, but higher compared with a study utilizing HA for buttock augmentation. Reported expected post-treatment events were mostly mild with maximum incidence between day(s) 1 to 3 and soreness as the most common event. The incidence of expected post-treatment events were, in similarity with the AEs, higher compared with when the HA gel was used for buttock augmentation. The reasons for the discrepancy in AE and expected post-treatment event incidences between those studies and present work are not known but may reflect differences in target tissues cover. In the sternal area, the cover is very thin compared with the buttocks, and smaller irregularities due to capsular contracture are likely to be more palpable. In a previous study using the product in the female breast, capsular formation with firmness was noted in 25% of patients. In the current study, 30% had firmness of the products. From the 9 patients from the Swedish site that did not consent to re-treatment, only one made this decision due to an AE (central accumulation).

Possible study limitations included the use of a subpopulation of PE patients, somewhat restricting generalizability of results, and that objective evaluations on the aesthetic outcome of patients’ chest were not carried out.

**CONCLUSIONS**

The HA gel treatment for PE improved patients’ quality of life and the perceived look of their chest and may thus constitute a treatment option for mild PE cases owing to the well-tolerated intervention. As with many other nonsurgical procedures, it may also have much greater patient acceptance than a surgical intervention and act as a door opener to later surgical procedures, as experience noted after HA injections to enhance the female breast.

**Supplementary Material**

This article contains supplementary material located online at www.aestheticsurgeryjournal.com.
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REFERENCES

1. Kelly RE Jr, Lawson ML, Paidas CN, Hruban RH. Pectus excavatum in a 112-year autopsy series: anatomic findings and the effect on survival. J Pediatr Surg. 2005;40(8):1275-1278.
2. Ji Y, Liu W, Chen S, et al. Assessment of psychosocial functioning and its risk factors in children with pectus excavatum. Health Qual Life Outcomes. 2011;9:28.
3. Kelly RE Jr, Cash TF, Shamberger RC, et al. Surgical repair of pectus excavatum markedly improves body image and perceived ability for physical activity: multicenter study. Pediatrics. 2008;122(6):1218-1222.
4. Ohno K, Morotomi Y, Nakahira M, et al. Indications for surgical repair of funnel chest based on indices of chest wall deformity and psychological state. Surg Today. 2003;33(9):662-665.
5. Brochhausen C, Turial S, Müller FK, et al. Pectus excavatum: history, hypotheses and treatment options. Interact Cardiovasc Thorac Surg. 2012;14(6):801-806.
6. Hebra A. Minimally invasive repair of pectus excavatum. Semin Thorac Cardiovasc Surg. 2009;21(1):76-84.
7. Krasopoulos G, Goldstraw P. Minimally invasive repair of pectus excavatum deformity. Eur J Cardiothorac Surg. 2011;39(2):149-158.
8. Kelly RE Jr. Pectus excavatum: historical background, clinical picture, preoperative evaluation and criteria for operation. Pediatr Surg Int. 2008;24(3):181-193.
9. Ravitch MM. The operative treatment of pectus excavatum. Ann Surg. 1949;129(4):429-444.
10. Nuss D, Kelly RE Jr, Croitoru DP, Katz ME. A 10-year review of a minimally invasive technique for the correction of pectus excavatum. J Pediatr Surg. 1998;33(4):545-552.
11. Pilegaard HK. Extending the use of Nuss procedure in patients older than 30 years. Eur J Cardiothorac Surg. 2011;40(2):334-337.
12. Krasopoulos G, Dusmet M, Ladas G, Goldstraw P. Nuss procedure improves the quality of life in young male adults with pectus excavatum deformity. Eur J Cardiothorac Surg. 2006;29(1):1-5.
13. Dzieliicki J, Korlacki W, Janicka I, Dzieliicka E. Difficulties and limitations in minimally invasive repair of pectus excavatum–6 years experiences with Nuss technique. Eur J Cardiothorac Surg. 2006;30(5):801-804.
14. Snel BJ, Sprock CA, Werker PM, van der Lei B. Pectus excavatum reconstruction with silicone implants: long-term results and a review of the english-language literature. Ann Plast Surg. 2009;62(2):205-209.
15. Margulis A, Sela M, Neuman R, Buller-Sharon A. Reconstruction of pectus excavatum with silicone implants. J Plast Reconstr Aesthet Surg. 2006;59(10):1082-1086.
16. Marks MW, Argenta LC, Lee DC. Silicone implant correction of pectus excavatum: indications and refinement in technique. Plast Reconstr Surg. 1984;74(1):52-58.
17. Lopez M, Patoir A, Costes F, Varlet F, Barthelemy JC, Tiffet O. Preliminary study of efficacy of cup suction in the correction of typical pectus excavatum. J Pediatr Surg. 2016;51(1):183-187.
18. Haecker FM. The vacuum bell for conservative treatment of pectus excavatum: the Basle experience. Pediatr Surg Int. 2011;27(6):623-627.
19. Smith KC. Reversible vs. nonreversible fillers in facial aesthetics: concerns and considerations. Dermatol Online J. 2008;14(8):3.
20. Lahiri A, Waters R. Experience with Bio-Alcamid, a new soft tissue endoprosthesis. J Plast Reconstr Aesthet Surg. 2007;60(6):663-667.
21. Krasopoulos G, Dusmet M, Ladas G, Goldstraw P. Nuss procedure improves the quality of life in young male adults with pectus excavatum–6 years experiences with Nuss technique. Eur J Cardiothorac Surg. 2006;30(5):801-804.
22. Haller JA Jr, Kramer SS, Liemet SA. Use of CT scans in selection of patients for pectus excavatum surgery: a preliminary report. J Pediatr Surg. 1987;22(10):904-906.
23. Raichura N, Entwisle J, Leverment J, Beardsmore CS. Breath-hold MRI in evaluating patients with pectus excavatum. Br J Radiol. 2001;74(884):701-708.
24. Lawson ML, Cash TF, Akers R, et al. A pilot study of the impact of surgical repair on disease-specific quality of life among patients with pectus excavatum. J Pediatr Surg. 2003;38(6):916-918.
25. Ware JE Jr, Kosinski M, Turner-Bowker DM, Sundaram M, Gandek B, Mariuham ME. SF-12v2 Health Survey: Administration Guide for Clinical Trial Investigators. Lincoln, RI: QualityMetric Incorporated; 2009.
30. EuroQol Group. EuroQol--a new facility for the measurement of health-related quality of life. *Health Policy*. 1990;16(3):199–208.

31. Sivathasan N, Chakrabarty KH. A simple idea for approximating the volume of filler needed for chest-wall contour-defects. *J Cosmet Dermatol*. 2012;11(3):235-236.

32. Steinmann C, Krille S, Mueller A, Weber P, Reingruber B, Martin A. Pectus excavatum and pectus carinatum patients suffer from lower quality of life and impaired body image: a control group comparison of psychological characteristics prior to surgical correction. *Eur J Cardiothorac Surg*. 2011;40(5):1138-1145.