SURGICAL (J KARPELOWSKY, SECTION EDITOR)



Less Is More: Recent Evolutions in Paediatric Surgery

Craig A McBride^{1,2} · Bhaveshkumar Patel^{1,2}

Published online: 18 May 2017 © Springer Science + Business Media New York 2017

Abstract

Purpose of Review The purpose of this study was to examine some recent developments in paediatric surgery, to both highlight them and to illustrate an underlying theme.

Recent Findings Paediatric surgeons have a desire to minimise morbidity, recognising the potential fragility of the child surrounding the disease. Modern solutions continue to address underlying pathologies, but with lower morbidity to the surrounding child. Laparoscopic surgery is an obvious example of this. It is not the only example. The move from open to percutaneous approaches for central venous access and tumour biopsy is another illustration. In some cases, an operation may not be required at all, such as treating empyema with fibrinolytics rather than surgery.

Summary Minimising operations, minimising access, and in some cases not operating at all are underlying themes to an approach that seeks to minimise harm.

Keywords Primum non nocere · Central venous catheterisation · Empyema · Appendicitis, non-operative management

This article is part of the Topical Collection on Surgical

Craig A McBride cmcbride@paedsurgery.com

¹ Surgical Team: Infants, Toddlers, Children (STITCh), Lady Cilento Children's Hospital, 501 Stanley Street, South Brisbane, QLD 4101, Australia

² Centre for Children's Burns and Trauma Research, Queensland Children's Medical Research Institute, University of Queensland, St Lucia, QLD, Australia

Introduction

The aphorism 'primum non nocere' can be translated as 'firstly, do no harm'. It is often mentioned in relation to medicine but is a difficult philosophy to adhere to in surgical specialties. The very nature of surgery means some harm to normal tissues is inevitable, as the surgeon approaches their target tissue. A more appropriate surgical maxim would be 'primum quam minime nocere', which translates as 'firstly do as little harm (as possible)'. Paediatric surgeons have a desire to minimise harm to the child surrounding the disease. Surgery has the capacity not only for great benefit but also great harm. The challenge is to effect the former while minimising the latter. This is especially important in children, since the surgeon is working with a growing and changing canvas. For the smallest infants, that canvas is fragile, and anything that reduces surgical harm is desirable.

Surgical harm can be decreased in a number of ways. Surgeons can minimise their approach to the target tissue, thereby causing less trauma to normal tissues. They can adopt a minimal approach to surgery once there, doing the least necessary to solve the problem. In some cases, surgeons have discovered that they may not need to operate at all, as research and experience challenge previously held beliefs about the benefit of some procedures. Paediatric surgeons continue to explore these approaches, with a view to minimising harm to their patients.

One historical example to illustrate the concept of 'primum quam minime nocere' is the evolution of surgical approaches to idiopathic hypertrophic pyloric stenosis (IHPS). William E. Ladd called surgery for IHPS "... among the most satisfactory procedures in the surgical field." Direct attack on the pylorus was initially highly invasive, with finger divulsion (Loreta's procedure) or even pylorectomy [1]. Heineke (in 1886) and Mikuliz (in 1887) independently devised a full thickness pyloroplasty [2, 3]. Fredet and Weber in the early 1900s recognised that an extramucosal pyloroplasty was sufficient to treat the disease, avoiding the risk of spill of gastric contents in an era predating effective antibiotics [4, 5]. This was evolution by subtraction, minimising the operation to achieve the same outcome. Ramstedt further simplified the operation by recognising that re-apposition of the split pyloric muscle was unnecessary and that an extramucosal pyloromyotomy alone was sufficient, a further evolution by subtraction. That this operation is still performed over a century later attests to its longevity. While there have been further changes since Ramstedt, these centre on the approach to the pylorus rather than the operation itself. The large central abdominal incisions of the early part of the twentieth century have given way to trans-umbilical approaches, either open or laparoscopic. Once at the pylorus, the operation is the same-an extramucosal pyloromyotomy.

Minimising the Approach

A minimised approach to surgery has the aim of achieving the same goal at the target tissue, with decreased trauma to tissues encountered on the way. The most familiar example of a minimised approach is the rise of laparoscopic paediatric surgery, but it is not the only example. Another example is the increased use of percutaneous techniques.

A minimised approach means smaller scars, though parents are less concerned with the size of the scar than they are with potential complications [6]. Scars in children, particularly burn scars, can cause significant detriment to quality of life so strategies to reduce scarring mitigate this [7]. Scars in children can become more problematic as the child grows, particularly burn scars across joints. Wounds in neonates can tether as the child grows, leading to increasingly unsightly scarring.

Endosurgery

Endosurgery encompasses those approaches where the operator's view is via videoscopic equipment, rather than direct visualisation. The target may be accessed via natural orifices in the aerodigestive or genitourinary tract. It may also be approached via incisions in the abdomen or thorax—laparoscopic or thoracoscopic surgery. When the public think of minimisation in surgery, it is laparoscopy that often first comes to mind.

Surgeons worldwide enthusiastically adopted laparoscopic surgery, often in advance of high-quality studies demonstrating a benefit. Single-incision laparoscopic surgery (SILS) is essentially a modification of this technique. In SILS, a single wound is created for a laparoscopic approach. This compromises the natural triangulation of multi-port laparoscopic surgery, but developments in instrument design have to some extent compensated for this. The perceived advantage is a single incision and therefore even less scarring. This incision is larger and has, to some extent, been offset by the availability of smaller laparoscopic instruments (3 mm or smaller), and therefore smaller scars. Paediatric surgeons have not adopted SILS as enthusiastically as their adult colleagues, perhaps because the perceived marginal scar benefit does not offset the increased difficulty (and therefore risk) of the operation. A 2.5-cm SILS port incision for an adult surgeon can be a laparotomy wound for a paediatric surgeon.

Most paediatric surgical operations are achievable laparoscopically or thoracoscopically. In many cases, such as oesophageal atresia repair, there is a body of evidence demonstrating at least equivalent results [8]. Laparoscopic surgery for biliary atresia is an exception. A number of high-volume centres adopted a laparoscopic approach, while continuing to analyse their results. The operation was shown to be technically feasible laparoscopically, but systematic reviews demonstrated worse outcomes [9••, 10•]. Biliary atresia remains one of the few operations to have demonstrably worse outcomes with laparoscopic, compared to open, approaches. *Primum quam minime nocere* for biliary atresia means the current gold standard remains an open approach. The open approach currently has better long-term results for biliary drainage and native liver survival.

Central Venous Access

More severe diseases require more intensive treatments. This is particularly so in neonatal and paediatric intensive care, and in paediatric oncology [11]. Central venous access devices as small as 1 French (1Fr/28G) are now routinely available, meaning they can be deployed in smaller and smaller children. Minimisation has not solely occurred in terms of the size of these devices, but also in the techniques associated with their insertion and aftercare. The size of the inserted device appears to alter complication rates, particularly in patients under 5 years of age where lines smaller than 6Fr are safer [12].

Surgeons previously, and of necessity, became adept at finding points of venous cut-down [13]. Choice of insertion techniques has undergone minimisation, with a move away from open cut-down to percutaneous techniques, with or without ultrasound guidance. There are mixed data on the use of ultrasound-guided (either real time or using prelocation) over landmark-guided (or 'blind') techniques. Data from the anaesthetic literature suggests landmark insertion techniques to be safe with high success rates [14]. With smaller children, larger lines and less-experienced operators, the chances of success decline [14]. Recent reviews demonstrate lower failure rates with ultrasound-guided techniques [15, 16]. Previously open surgical cut-down was the norm, with an up to 25% occurrence of permanent vein occlusion following removal [17••]. The equivalent rate for ultrasound-guided percutaneous insertion is 3%, which has obvious implications in children requiring lifelong central venous access [17••]. Percutaneous ultrasound-guided techniques may have longer intraoperative screening times that need to be offset against the advantages of smaller scars and higher vein patency post-removal of the line [18].

Peripherally inserted central catheters (PICCs) were first described in 1975 as an alternative method of central venous access [19]. There is wide interhospital variation in the use of PICCs in settings such as complicated appendicitis [20]. Risk factors for complications such as thrombosis are being defined and appear to approach those of surgical central lines [21]. Numbers being inserted are increasing and dwell times are decreasing, due either to complications necessitating early removal or to shorter planned treatments. It is not clear the associated complications are fully appreciated by referring clinicians, who may see PICCs as a handy alternative to multiple and sequential peripheral intravenous lines [22]. Approximately 20% of patients with complicated appendicitis will now have a PICC line, with no appreciable change in outcomes [23]. This is perhaps an area where minimisation is viewed differently by paediatricians compared to surgeons or anaesthetists. For the former, the patient arrives back from theatre with a PICC line in situ and junior members of the team no longer have to struggle with inserting intravenous lines. For the latter, inserting a PICC may represent an hour or more of theatre time for no appreciable reduction in complication risks [23]. The appropriate indications and optimum management of PICC lines are yet to be determined, but they have the potential to streamline treatment for some groups of patients.

Tumour Biopsy

The majority of long-term central venous access devices are in children with malignancies. It is not always possible to make a diagnosis from history, examination, and imaging. Preoperative chemotherapy has the potential to cause tumour shrinkage and make resection less morbid, but there is a risk of causing harm by delivering suboptimal chemotherapy. A biopsy allows confirmation of diagnosis and appropriate targeting of neoadjuvant therapy but carries a risk of harm from the biopsy itself. Children's cancer groups have taken varying approaches to this conundrum, based in part upon their early history with the tumours they encountered [24]. For some, upfront resection of the mass is the standard of care. For others, neoadjuvant chemotherapy, with or without prior biopsy, is more common. In situations where a biopsy is performed, there has been a move towards percutaneous core biopsy for most childhood tumours. Percutaneous biopsy accuracy and yields are improved with multiple passes, and with the use of immunohistochemical techniques [25, 26]. Smaller amounts of tissue are needed to make an accurate diagnosis that includes prognostic variables. There are now a multitude of prognostic factors employed in both Children's Oncology Group (COG) and International Society of Paediatric Oncology (SIOP) protocols. For example, Wilms' tumour accepted parameters include loss of heterozygosity on chromosomes 1p and 16q [27]. Future studies may incorporate gain of chromosome 1q, the methylation pattern of chromosome 11p15, and molecular markers for resistant blastema into risk classification schemata [27]. The net effect is the increasing ability to more accurately risk-stratify patients. This permits minimisation of neoadjuvant or adjuvant therapy, with no detrimental effects on cure rates but a correspondingly beneficial decrease in long-term secondary effects.

Interventional Radiology

Interventional radiology in paediatric surgery has grown in scope and indication. Image-guided approaches are not only being utilised in radiology, as surgeons and anaesthetists also use ultrasound scanning in line placements. Interventional radiological approaches are well documented not only for central line placement but also for indications such as gastrostomy or ventriculoatrial shunt placement [28•, 29]. Radiological ablation for tumours—primary, recurrent and metastatic—is also showing some promise as a treatment modality [30]. Antegrade sclerotherapy for varicocele has recurrence rates as low as 3.4%, without the attendant risk of hydrocele formation [31].

Minimising the Operation

The contemporary approach to empyema minimises not only the approach but also the operation. The importance of draining pus from the pleural cavity has been known since the days of Hippocrates [32]. The morbidity of thoracotomy and decortication led many centres to adopt video-assisted thoracic surgery (VATS) for empyema. VATS became the treatment of choice with evidence showing better results than tube thoracostomy or non-operative management [33, 34].

Not satisfied with VATS, the approach to empyema is being further minimised with the use of fibrinolytic therapy [35••]. Results of trials comparing VATS with fibrinolytic therapy show equivalence in outcome [36–39]. Fibrinolytic therapy allows placement of a small calibre tube, potentially under conscious sedation rather than full general anaesthesia. Centres are now using this therapy as first line in their approach to pleural empyema, with promising results [40, 41]. There are treatment failures with fibrinolytic therapy, but it is currently difficult to predict a priori which patients these might be [42]. Despite these studies, choice of first-line therapy is predicted by the specialty of the clinician deciding, and there is a general agreement that the published evidence is inconclusive [43].

Not Operating at All

The appropriateness of a number of operations is now questionable, either due to advances in non-surgical care or by a growing recognition that those operations do not necessarily afford significant or lasting benefit. Splenectomy was previously a common treatment for blunt splenic trauma, until studies in the late 1960s and early 1970s showed it was possible to treat children successfully without splenectomy [44, 45]. This approach has now been extended to other intraabdominal solid organs, and to adult patients [46]. Potentially disfiguring surgery for vascular anomalies has given way to medical therapies such as propranolol for infantile haemangiomas. Those medical therapies in turn have seen dose minimisation studies demonstrating equal benefit with improved side effect profiles [47].

Appendicitis has also recently come under scrutiny. For over a century, the accepted treatment for appendicitis has been an appendicectomy. As a single operation, appendicectomy makes up 8.2% of all general paediatric operations [48]. Though common, this operation is not without risk. Between 6 and 15% of patients will not have appendicitis at all, resulting in an unnecessary operation [49]. There are also the attendant risks of post-operative infection, ileus, and readmission. In children with an appendiceal phlegmon, there is an evidence base to treating with antibiotics, rather than with an up-front appendicectomy [50, 51]. Surgeons have now begun to formally question the previously accepted paradigm and are extending non-operative management of appendicitis to all patients. Recent literature on this topic suggests such an approach will be successful in 87.5–98.7% of patients. To date, there has been one published randomised pilot study and several cohort studies [52-56]. A number of centres are in the process of conducting randomised controlled trials comparing operative with non-operative management of appendicitis in children.

Conclusion

Paediatric surgery continues to explore new ways of achieving the same or improved outcomes for patients. The overarching philosophy is to minimise harm without compromising the aim of the operation. This can be achieved by refining the operation to its bare minimum, by minimising the approach through normal tissues, and in some cases, by challenging the accepted paradigm that an operation is necessary at all. These three elements are often blended in contemporary surgeons' approach to paediatric disease. Acknowledgements We are grateful for the advice on the accurate construction of the Latin dictum *Primum quam minime nocere*, meaning 'firstly do as little harm (as possible)', to Emeritus Professor Robert Milns AM, BA(Hons) *Leeds*, MA *Camb*, Hon.DLitt *Qld* and to Dr. John Ratcliffe, PhD(Classics) *Qld*, FRCSEd, FRCR. Honorary Research Fellow *Qld*.

Compliance with Ethical Standards

Conflict of Interest Craig A McBride and Bhaveshkumar Patel declare no potential conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:

- · Of importance
- •• Of major importance
- Coombe RVI. Congenital hypertrophic stenosis of the pylorus. Ann Surg. 1911;54:167–73.
- 2. Mikulicz J. Zur operativen Behandlung des stenosirenden Magenschwures. Arch Klin Chir. 1888;37:79–90.
- 3. Heineke MR. Abdominal operations. N Y. 1886;1961:169.
- DuFour H, Fredet P. La stenose hypertrophique du pylore chez le nourrisson et son traitment chirugical. Rev Chir. 1908;37:208–53.
- Weber W. Über eine technische Neuerung bei der Operation der Pylorusstenose des Säuglings. Berliner klin Wochenschr. 1910: 763–5.
- Niyogi A, Clarke SA. Elective paediatric surgery: what do parents really want to know? Scott Med J. 2012;57:65–8.
- Maskell J, Newcombe P, Martin G, Kimble R. Psychosocial functioning differences in pediatric burn survivors compared with healthy norms. J Burn Care Res. 2013;34:465–76.
- Rothenberg S. Thoracoscopic repair of esophageal atresia and tracheo-esophageal fistula in neonates: the current state of the art. Pediatr Surg Int. 2014;30:979–85.
- 9.•• Lishuang M, Zhen C, Guoliang Q, Zhen Z, Chen W, Long L, et al. Laparoscopic portoenterostomy versus open portoenterostomy for the treatment of biliary atresia: a systematic review and metaanalysis of comparative studies. Pediatr Surg Int. 2015;31:261–9. Meta-analysis of 11 studies, showing no significant differences in intraoperative and early postoperative outcomes, but a lower 2-year native liver survival with the laparoscopic approach to Kasai portoenterostomy
- 10.• Hussain MH, Alizai N, Patel B. Outcomes of laparoscopic Kasai portoenterostomy for biliary atresia: a systematic review. J Pediatr Surg. 2017;52:264–7. Ten studies demonstrating the same findings as the systematic review and meta-analysis above
- Ainsworth S, McGuire W. Percutaneous central venous catheters versus peripheral cannulae for delivery of parenteral nutrition in neonates. Cochrane Database Syst Rev. 2015:CD004219.
- Janik JE, Conlon SJ, Janik JS. Percutaneous central access in patients younger than 5 years: size does matter. J Pediatr Surg. 2004;39:1252–6.
- Iserson KV, Criss EA. Pediatric venous cutdowns: utility in emergency situations. Pediatr Emerg Care. 1986;2:231–4.

- Malbezin S, Gauss T, Smith I, Bruneau B, Mangalsuren N, Diallo T, et al. A review of 5434 percutaneous pediatric central venous catheters inserted by anesthesiologists. Paediatr Anaesth. 2013;23:974– 9.
- Shime N, Hosokawa K, MacLaren G. Ultrasound imaging reduces failure rates of percutaneous central venous catheterization in children. Pediatr Crit Care Med. 2015;16:718–25.
- Costello JM, Clapper TC, Wypij D. Minimizing complications associated with percutaneous central venous catheter placement in children: recent advances. Pediatr Crit Care Med. 2013;14:273–83.
- 17.•• Wragg RC, Blundell S, Bader M, Sharif B, Bennett J, Jester I, et al. Patency of neck veins following ultrasound-guided percutaneous Hickman line insertion. Pediatr Surg Int. 2014;30:301–4. This paper demonstrates lower vein occlusion rates after line removal following percutaneous lines (3%) compared to rates after open approaches (up to 25% vein occlusion rate)
- Friend J, Lindsey-Temple S, Gollow I, Whan E, Gera P. Review of the radiation exposure during screening of surgically implanted central venous access devices. J Pediatr Surg. 2015;50:1214–9.
- Hoshal VLJ. Total intravenous nutrition with peripherally inserted silicone elastomer central venous catheters. Arch Surg. 1975;110: 644–6.
- Rice-Townsend S, Barnes JN, Hall M, Baxter JL, Rangel SJ. Variation in practice and resource utilization associated with the diagnosis and management of appendicitis at freestanding children's hospitals: implications for value-based comparative analysis. Ann Surg. 2014;259:1228–34.
- Kanin M, Young G. Incidence of thrombosis in children with tunneled central venous access devices versus peripherally inserted central catheters (PICCs). Thromb Res. 2013;132:527–30.
- Gibson C, Connolly BL, Moineddin R, Mahant S, Filipescu D, Amaral JG. Peripherally inserted central catheters: use at a tertiary care pediatric center. J Vasc Interv Radiol. 2013;24:1323–31.
- Sulkowski JP, Asti L, Cooper JN, Kenney BD, Raval MV, Rangel SJ, et al. Morbidity of peripherally inserted central catheters in pediatric complicated appendicitis. J Surg Res. 2014;190:235–41.
- Gleason JM, Lorenzo AJ, Bowlin PR, Koyle MA. Innovations in the management of Wilms' tumor. Ther Adv Urol. 2014;6:165–76.
- Blondiaux E, Laurent M, Audureau E, Boudjemaa S, Sileo C, Lenoir M, et al. Factors influencing the diagnostic yield and accuracy of image-guided percutaneous needle biopsy of pediatric tumors: single-center audit of a 26-year experience. Pediatr Radiol. 2016;46:372–82.
- Acord M, Shaikh R. Predictors of diagnostic success in imageguided pediatric soft-tissue biopsies. Pediatr Radiol. 2015;45: 1529–34.
- Dome JS, Perlman EJ, Graf N. Risk stratification for Wilms tumor: current approach and future directions. Am Soc Clin Oncol Educ Book. 2014;34:215–23.
- 28.• Crowley JJ, Hogan MJ, Towbin RB, Saad WE, Baskin KM, Marie Cahill A, et al. Quality improvement guidelines for pediatric gastrostomy and gastrojejunostomy tube placement. J Vasc Interv Radiol. 2014. pp. 1983–91. Comprehensive consensus statement regarding interventional radiological placement of gastrostomy tubes.
- 29. Clark DJ, Chakraborty A, Roebuck DJ, Thompson DNP. Ultrasound guided placement of the distal catheter in paediatric ventriculoatrial shunts-an appraisal of efficacy and complications. Childs Nerv Syst. 2016;32:1219–25.
- Gómez FM, Patel PA, Stuart S, Roebuck DJ. Systematic review of ablation techniques for the treatment of malignant or aggressive benign lesions in children. Pediatr Radiol. 2014;44:1281–9.
- Paradiso FV, Mason EJ, Nanni L. Antegrade sclerotherapy to treat all types of varicoceles in the pediatric population: experience of a single center. Urology. 2016;98:149–53.

- 32. Heffner JE. Multicenter trials of treatment for empyema—after all these years. N Engl J Med. 2005;352:926–8.
- Kurt BA, Winterhalter KM, Connors RH, Betz BW, Winters JW. Therapy of parapneumonic effusions in children: video-assisted thoracoscopic surgery versus conventional thoracostomy drainage. Pediatrics. 2006;118:e547–53.
- Avansino JR, Goldman B, Sawin RS, Flum DR. Primary operative versus nonoperative therapy for pediatric empyema: a meta-analysis. Pediatrics. 2005;115:1652–9.
- 35.•• Krenke K, Peradzyńska J, Lange J, Ruszczyński M, Kulus M, Szajewska H. Local treatment of empyema in children: a systematic review of randomized controlled trials. Acta Paediatr. 2010;99: 1449–53. This 4 RCT review shows equivalent outcomes with VATS vs fibrinolytics and improved outcomes for fibrinolytics vs placebo
- St Peter SD, Tsao K, Spilde TL, Keckler SJ, Harrison C, Jackson MA, et al. Thoracoscopic decortication vs tube thoracostomy with fibrinolysis for empyema in children: a prospective, randomized trial. J Pediatr Surg. 2009;44:106–11. discussion111
- 37. Sonnappa S. Urokinase and VATS are equally effective for septated empyema. J Pediatr. 2015;166:1320–1.
- Sonnappa S, Cohen G, Owens CM, van Doorn C, Cairns J, Stanojevic S, et al. Comparison of urokinase and video-assisted thoracoscopic surgery for treatment of childhood empyema. Am J Respir Crit Care Med. 2006;174:221–7.
- Marhuenda C, Barceló C, Fuentes I, Guillén G, Cano I, López M, et al. Urokinase versus VATS for treatment of empyema: a randomized multicenter clinical trial. Pediatrics. 2014;134:e1301–7.
- Gasior AC, Knott EM, Sharp SW, Ostlie DJ, Holcomb GW, St Peter SD. Experience with an evidence-based protocol using fibrinolysis as first line treatment for empyema in children. J Pediatr Surg. 2013;48:1312–5.
- Livingston MH, Colozza S, Vogt KN, Merritt N, Bütter A. Making the transition from video-assisted thoracoscopic surgery to chest tube with fibrinolytics for empyema in children: any change in outcomes? Can J Surg. 2016;59:167–71.
- Livingston MH, Cohen E, Giglia L, Pirrello D, Mistry N, Mahant S, et al. Are some children with empyema at risk for treatment failure with fibrinolytics? A multicenter cohort study. J Pediatr Surg. 2016;51:832–7.
- Richards MK, Mcateer JP, Edwards TC, Hoffman LR, Kronman MP, Shaw DW, et al. Establishing equipoise: national survey of the treatment of pediatric para-pneumonic effusion and empyema. Surg Infect (Larchmt). 2016:sur.2016.134.
- 44. Upadhyaya P, Simpson JS. Splenic trauma in children. Surg Gynecol Obstet. 1968;126:781–90.
- 45. Douglas GJ, Simpson JS. The conservative management of splenic trauma. J Pediatr Surg. 1971;6:565–70.
- Holland AJ, McBride CA. Non-operative advances: what has happened in the last 50 years in paediatric surgery? J Paediatr Child Health. 2015;51:74–7.
- 47. Tan CE, Itinteang T, Leadbitter P, Marsh R, Tan ST. Low-dose propranolol regimen for infantile haemangioma. J Paediatr Child Health. 2015;51:419–24.
- Wilson BE, Cheney L, Patel B, Holland AJA. Appendicectomy at a children's hospital: what has changed over a decade? ANZ J Surg. 2012;82:639–43.
- Flum DR, Morris A, Koepsell T, Dellinger EP. Has misdiagnosis of appendicitis decreased over time? A population-based analysis. JAMA. 2001;286:1748–53.
- St Peter SD, Aguayo P, Fraser JD, Keckler SJ, Sharp SW, Leys CM, et al. Initial laparoscopic appendectomy versus initial nonoperative management and interval appendectomy for perforated appendicitis with abscess: a prospective, randomized trial. J Pediatr Surg. 2010;45:236–40.

- Lee SL, Islam S, Cassidy LD, Abdullah F, Arca MJ. 2010 American pediatric surgical association outcomes and clinical trials committee. Antibiotics and appendicitis in the pediatric population: an American pediatric surgical association outcomes and clinical trials committee systematic review. J Pediatr Surg. 2010;45:2181–5.
- 52. Svensson JF, Patkova B, Almström M, Naji H, Hall NJ, Eaton S, et al. Nonoperative treatment with antibiotics versus surgery for acute nonperforated appendicitis in children: a pilot randomized controlled trial. Ann Surg. 2015;261:67–71.
- Tanaka Y, Uchida H, Kawashima H, Fujiogi M, Takazawa S, Deie K, et al. Long-term outcomes of operative versus nonoperative treatment for uncomplicated appendicitis. J Pediatr Surg. 2015;50: 1893–7.
- Minneci PC, Mahida JB, Lodwick DL, Sulkowski JP, Nacion KM, Cooper JN, et al. Effectiveness of patient choice in nonoperative vs surgical management of pediatric uncomplicated acute appendicitis. JAMA Surg. 2016;151:408–15.
- Hartwich J, Luks FI, Watson-Smith D, Kurkchubasche AG, Muratore CS, Wills HE, et al. Nonoperative treatment of acute appendicitis in children: a feasibility study. J Pediatr Surg. 2016;51:111–6.
- 56. Gorter RR, van der Lee JH, Cense HA, Kneepkens CMF, Wijnen MHWA, In't Hof KH, et al. Initial antibiotic treatment for acute simple appendicitis in children is safe: short-term results from a multicenter, prospective cohort study. Surgery. 2015;157:916–23.