

The influence of the COVID-19 pandemic on the management of pediatric appendicitis; an international study

CONNECT-study

Paul van Amstel¹, MD, Ali El Ghazzaoui², MD, Nigel J. Hall³, MD PhD, Tomas Wester^{4,5}, MD PhD, Francesco Morini⁶, MD, Johanna H. van der Lee⁷, MD PhD, Georg Singer, MD PhD⁸, Agostino Pierro^{2,9}, MD PhD, Augusto Zani^{2,9}, MD PhD, Ramon R. Gorter¹, MD PhD; on behalf of the CONNECT collaborative study group

1. Department of Pediatric Surgery, Emma Children's Hospital, Amsterdam UMC, University of Amsterdam & Vrije Universiteit Amsterdam, Amsterdam, the Netherlands. rr.gorter@amsterdamumc.nl
2. Division of General and Thoracic Surgery, Hospital for Sick Children, Toronto, Ontario, Canada. elghazzaoui.ali@gmail.com / agostino.pierro@sickkids.ca / augusto.zani@sickkids.ca
3. University Surgery Unit, Faculty of Medicine, University of Southampton, Southampton, United Kingdom. n.j.hall@soton.ac.uk
4. Department of Pediatric Surgery, Astrid Lindgren Children's Hospital, Karolinska University Hospital, Stockholm, Sweden. tomas.wester@ki.se
5. Department of Women's and Children's health, Karolinska Institutet, Stockholm, Sweden
6. Neonatal Surgery Unit, Medical and Surgical Department of the Fetus, Newborn, and Infant, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy. francesco.morini@opbg.net
7. Amsterdam UMC, University of Amsterdam & Vrije Universiteit Amsterdam, Pediatric Clinical Research Office, Amsterdam, and Knowledge Institute of the Dutch Association of Medical Specialists, Utrecht, the Netherlands. h.vanderlee@kennisinstituut.nl
8. Department of Paediatric and Adolescent Surgery, Medical University of Graz, Graz, Austria. georg.singer@medunigraz.at
9. Department of Surgery, University of Toronto, Toronto, ON, Canada

Correspondence:

Name: P. van Amstel, MD

Email: p.vanamstel@amsterdamumc.nl

Telephone: +31 20 56 65693

Fax: +31 20 444 2135

Abbreviations:

CI: Confidence interval

EUPSA: European Pediatric Surgeons' Association

IAA: Intra-abdominal abscess

IQR: Interquartile range

NOT: Non-operative treatment

SSI: Surgical site infection

Introduction

The COVID-19 pandemic had a huge impact on healthcare system across the world forcing policymakers to reorganize hospital resources to increase capacity. Recommendations were made by surgical societies to postpone elective surgery and apply non-operative alternatives if available for surgical diseases.¹⁻³ The aim of our multicenter international study was to investigate the impact of the COVID-19 pandemic on pediatric appendicitis, specifically the proportion of children with complex appendicitis, alterations in the diagnostic work-up and treatment strategies and its outcomes.

Methods

An international retrospective study was conducted at 40 hospitals from 23 countries (supplement 1). The study was overseen by an international study steering group (RG/AZ/AP/NH/TW/FM/AG/PA) that developed the study protocol. This study was endorsed by the European Pediatric Surgeons' Association (EUPSA) which assisted in the recruitment of participating hospitals through the EUPSA Network Office. Principal investigators of participating sites obtained local ethical approval in accordance with local requirements. The study was reported according to the STROBE guidelines.⁴

Patients (<18 year) treated for acute appendicitis between January 2019 and December 2020 were screened for eligibility. Those treated non-operatively without imaging confirmed diagnosis of acute appendicitis were excluded. Diagnosis of acute appendicitis was defined as intraoperative and histopathological confirmation of appendicitis, and in case of non-operative treatment (NOT; see supplement 2 for definition) based on clinical, biochemical and radiological criteria. Local investigators were asked to define the start of the COVID-19 pandemic at their institution based on the start of the time period in which regular healthcare was affected by the pandemic. The COVID-group was defined as those patients treated between the start of the COVID period and December 31st, 2020. The control group

consisted of patients treated during the corresponding time period in 2019. To understand healthcare protocols and management strategies for acute appendicitis before and during the pandemic at each center, all participating sites were asked to complete a survey that was sent March 23rd, 2021. (Supplement 3)

Variables of interest and their definitions were agreed by the study steering group during protocol development and were based on the globally supported Core Outcome Set for studies reporting the treatment of acute simple appendicitis in children.⁵⁻⁸ Primary outcomes were the proportions of children treated for complex appendicitis, children that underwent imaging procedures for confirmation of appendicitis, children treated with non-surgical treatment strategies, and complications directly related to treatment. Secondary outcomes and definitions are displayed in supplement 2.

Comparative analyses were performed by calculating differences in proportions and 95% confidence intervals (CI). Subgroup analyses based on time period of presentation, age, and region were performed for appendicitis severity and complications. For all subgroup analyses, Bonferroni correction was applied to adjust for multiple testing. Statistics were performed using IBM SPSS statistics version 26 (IBM SPSS 26.0, Armonk, NY).

Results

Between January 2019 and December 2020 10655 children were treated for acute appendicitis, of which 2062 were excluded due to various reasons (Supplement 4). Therefore, 8593 patients were included, 4113 in the COVID-group and 4480 in the control group. Baseline characteristics of both groups were similar (Supplement 5).

The survey showed that, in the majority of participating centers, NOT and same day discharge were not standard of care during the pandemic and that there was no change in referral pathways or shift of patients with complex disease to the participating centers (Supplement 1).

Appendicitis severity

In the COVID-group 47.7% of patients were treated for complex appendicitis versus 45.0% in the control group (difference:2.7%;95%CI:0.6 to 4.8%; $p=0.014$) (Table 1). This increased proportion of complex appendicitis was only apparent during the first three months of the pandemic (difference:5.6%;95%CI:1.8 to 9.3%; $p=0.003$;adjusted $p=0.007$) and was predominantly caused by an absolute decrease of patients with simple appendicitis. The subgroup analysis based on region showed that the proportion of patients treated for complex appendicitis increased with 3.5% (95%CI:1.2 to 5.8%; $p=0.004$;adjusted $p=0.020$) in Europe. No significant differences were found for other continents (Table 2).

Diagnostic work-up and initial treatment

In the COVID-group 86.0% of children underwent imaging during diagnostic work-up compared to 84.4% in the control group (difference:1.6%;95%CI:0.1 to 3.1%; $p=0.037$).

During the pandemic, 7.7% of patients were treated non-operatively compared to 7.3% in the control period (difference:0.4%;95%CI:-0.7 to 1.5%; $p=0.495$). Outcomes of NOT are displayed in supplement 6.

Of those treated surgically, 74.3% in the COVID-group and 71.2% in the control group underwent laparoscopic appendectomy (difference:3.1%;95%CI:1.2 to 5.1%; $p=0.002$). (Table 1.)

Complications

Both the primary and subgroup analyses found no differences in the number of patients experiencing any complication between the COVID and control group, nor in the severity of

complications. In both groups, an intra-abdominal abscess was the most frequent postoperative complication. (Table 1/2.)

Discussion

This international study found that the number of patients presenting with simple appendicitis decreased during the first months of the pandemic, resulting in a higher proportion of complex appendicitis compared to the control period. The proportion of patients treated non-operatively and the proportion of complications were comparable to the control period.

Several small single center studies have reported contradicting results on the influence of the pandemic on the proportion of patients treated for complex appendicitis. Some showing increased proportions of complex appendicitis (7-18%), whereas others could not detect any difference.⁹⁻¹⁴ In our study, the increased proportion of complex appendicitis seems to be the result of an absolute decrease of patients with simple appendicitis. A possible explanation could be the resolution of mild cases of simple appendicitis that did not seek medical care and recovered spontaneously or were treated with antibiotics by general practitioners.^{15, 16}

After the first months of the pandemic, proportions of simple and complex appendicitis were comparable to the control group, which was predominantly the result of an absolute increase of patients with simple appendicitis. This could be explained by the fact that the threshold to seek medical care for mild cases of appendicitis possibly decreased after the first months of the pandemic, as lockdown measures were slowly lifted and fear for COVID-19 declined. Our findings are in line with other population based studies that found an absolute decrease in both adult and pediatric patients presenting with simple appendicitis in the early pandemic period.¹⁷⁻¹⁹

This international multicenter study is limited by possible information and selection bias, which is inherent to retrospective selection of patients and data collection. Furthermore, the regional subgroup analysis was limited by a skewed distribution, as the majority of patients

were included in Europe. Lastly, our survey found no shift of patients with complex disease to participating centers, but this might still have occurred.

Major strength of our study is the international collaboration and subsequent large sample size of more than 8500 patients. Further strengths are the usage of the international core outcome set for acute appendicitis, development of a study protocol with predefined definitions of variables of interest, and an objective definition of appendicitis severity based on surgical and histopathological criteria.

In conclusion, this large international study showed that during the first months of the COVID-19 pandemic the proportion of pediatric patients treated for complex appendicitis was higher compared to the control period in 2019, which was predominantly caused by an absolute decrease of patients presenting with simple appendicitis. The management and outcomes of patients with acute appendicitis were relatively unaffected by the pandemic, reflecting the resilience of the participating centers.

Conflict of Interest Disclosures (including financial disclosures): The authors have no conflicts of interest to disclose for the submitted work.

Funding/Support: Tomas Wester received a grant from the Swedish Medical Research Council.

Role of Funder/Sponsor: The Swedish Medical Research Council had no role in any part of the study.

Acknowledgements

This study was endorsed by the European Pediatric Surgeons' Association (EUPSA) and participating hospitals were mainly recruited via the EUPSA Network Office. Requests for

data sharing will be considered by study steering group upon written request to the corresponding author. Deidentified participant data will be made available after receipt of a written proposal and a signed data sharing agreement.

Contributors' Statement Page

Paul van Amstel: Study conception, protocol development, study coordination, data collection, data verification, data interpretation, data analysis, writing of the manuscript (original draft, review and editing)

Ali El Ghazzaoui: Study conception, protocol development, study coordination, data collection, data interpretation, writing of the manuscript (original draft, review and editing)

Nigel J. Hall: Study conception, protocol development, study coordination, data collection, data interpretation, writing of the manuscript (original draft, review and editing)

Tomas Wester: Study conception, protocol development, study coordination, data collection, data interpretation, writing of the manuscript (original draft, review and editing)

Francesco Morini: Study conception, protocol development, study coordination, data collection, data interpretation, writing of the manuscript (original draft, review and editing)

Johanna H van der Lee: Data interpretation, data analysis, writing of the manuscript (original draft, review and editing)

Georg Singer: Data collection, data interpretation, writing of the manuscript (review and editing)

Agostino Pierro: Study conception, protocol development, study coordination, data collection, data interpretation, writing of the manuscript (original draft, review and editing)

Augusto Zani: Study conception, protocol development, study coordination, data collection, data interpretation, writing of the manuscript (original draft, review and editing)

Ramon R. Gorter: Study conception, protocol development, study coordination, data collection, data verification, data interpretation, data analysis, writing of the manuscript (original draft, review and editing)

CONNECT collaborative study group: Data collection, data interpretation, writing of the manuscript (review and editing)

The authors of the CONNECT study steering group had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Collaborators (CONNECT collaborative study group)

Prof. Martin L. Metzelder, MD PhD, Department of Pediatric Surgery, Medical University of Vienna, Waehringer Gürtel 18-20, 1090 Vienna, Austria.

martin.metzelder@meduniwien.ac.at

Sophie Langer, MD, Department of Pediatric Surgery, Medical University of Vienna, Waehringer Gürtel 18-20, 1090 Vienna, Austria. sophie.langer@meduniwien.ac.at

Prof. Ashrarur R Mitul, MS (Pediatric Surgery), Department of Pediatric Surgery, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh ashrarur@gmail.com

Dr. Sabbir Karim, MS (Pediatric Surgery), Department of Pediatric Surgery, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh

Dr. Nazmul Islam, MS (Pediatric Surgery), Department of Pediatric Surgery, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh

Anna Poupalou, MD PhD, Department of Pediatric Surgery, Université Libre de Bruxelles (ULB), HUDERF Hospital (Hôpital Universitaire des Enfants Reine Fabiola), Brussels, Belgium. apoupalou@gmail.com

Prof. Marc Miserez, MD PhD, Department of Abdominal Surgery, University Hospital Gasthuisberg KULeuven, Leuven, Belgium. marc.miserez@uzleuven.be

Edward Willems, MD, Department of Abdominal Surgery, University Hospital Gasthuisberg, KULeuven, Leuven, Belgium. edward.willems@uzleuven.be

Erika V. P. Ortolan, MD PhD, Associate Professor of Pediatric Surgery, Botucatu Medical School, Unesp. erika.ortolan@unesp.br

Pedro Luiz Toledo de Arruda Lourenção, MD PhD, Associate Professor of Pediatric Surgery, Botucatu Medical School, Unesp

Mark Bremholm Ellebæk, MD PhD, Surgical Research Unit, Odense University Hospital, University of Southern Denmark, Odense C, Denmark. Mark.Ellebaek1@rsyd.dk

Susanna Petersen, MD, Surgical Research Unit, Odense University Hospital, Odense C, Denmark. Susanna.Petersen@rsyd.dk

Janne Suominen, MD PhD, Department of Pediatric Surgery, New Children's Hospital, University of Helsinki and Helsinki University Hospital, Helsinki, Finland.

Janne.Suominen@hus.fi

Mikko Pakarinen, MD PhD, Department of Pediatric Surgery, New Children's Hospital, University of Helsinki and Helsinki University Hospital, Helsinki, Finland.

Mikko.Pakarinen@hus.fi

Françoise Schmitt, MD PhD, Department of Pediatric Surgery, University Hospital of Angers, Angers, France. FrSchmitt@chu-angers.fr

Prof. Arnaud Bonnard, MD PhD, Department of Pediatric Surgery and Urology, Robert Debré Children University Hospital, APHP, Paris University, Paris, France.

arnaud.bonnard@aphp.fr

Louise Montalva, MD, Department of Pediatric Surgery and Urology, Robert Debré Children University Hospital, APHP, Paris University, Paris, France. Louise.MONTALVA@aphp.fr

Garance Martin, MD, Department of Pediatric Surgery and Urology, Robert Debré Children University Hospital, APHP, Paris University, Paris, France. GARANCE.MARTIN@aphp.fr

Antonella Nahom di Veroli, MD, Department of Pediatric Surgery, Soroka Medical Center, Beer Sheva, Israel. anahom26@yahoo.it

Zaki Assi, MD, Department of Pediatric Surgery, Soroka Medical Center, Beer Sheva, Israel.

ZAKIAS@clalit.org.il

Alessio Pini-Prato, MD, Pediatric Surgery Unit, Umberto Bosio Center for Digestive Diseases, The Children Hospital, AO SS Antonio e Biagio e cesare Arrigo, Alessandria, Italy.

apini@ospedale.al.it

Ilaria Falconi, MD, Pediatric Surgery Unit, Umberto Bosio Center for Digestive Diseases, The Children Hospital, AO SS Antonio e Biagio e cesare Arrigo, Alessandria, Italy.

ilaria.falconi@ospedale.al.it

Prof. Daniele Alberti, MD, University of Brescia, Department of Pediatric Surgery- Children's Hospital, Brescia-Italy. daniele.alberti@unibs.it

Giovanni Boroni, MD, ASST Spedali Civili, Department of Pediatric Surgery, Brescia-Italy.

giovanni.boroni@unibs.it

Beatrice Montanaro, MD, University of Brescia, Department of Pediatric Surgery- Children's Hospital, Brescia-Italy. beatrice.montanaro01@gmail.com

Prof. Antonino Morabito, MD, University of Florence-Meyer Children's Hospital, Florence, Italy. antonino.morabito@unifi.it

Andrea Zulli, MD, University of Florence-Meyer Children's Hospital, Florence, Italy.

Riccardo Coletta MD PhD, University of Florence-Meyer Children's Hospital, Florence, Italy

Prof. Carmelo Romeo, MD, Department of Human Pathology of Adult and Childhood "Gaetano Barresi", Unit of Pediatric Surgery, University of Messina, Messina, Italy.

romeo.carmelo@unime.it

Enrica Antonelli, MD, Department of Human Pathology of Adult and Childhood "Gaetano Barresi", Unit of Pediatric Surgery, University of Messina, Messina, Italy

Francesca Nascimben, MD, Department of Human Pathology of Adult and Childhood
"Gaetano Barresi", Unit of Pediatric Surgery, University of Messina, Messina, Italy.

francescanascimben@gmail.com

Prof. Piergiorgio Gamba, MD, Pediatric Surgery Unit, Women's and Children's Health
Department, University of Padua, Padova, Italy. piergiorgio.gamba@unipd.it

Alberto Sgro, MD PhD, Pediatric Surgery Unit, Women's and Children's Health Department,
University of Padua, Padova, Italy. alberto.sgro@aopd.veneto.it

Alessandro Raffaele, MD, Pediatric Surgery Unit, Fondazione IRCCS Policlinico San Matteo,
University of Pavia, Pavia, Italy. A.Raffaele@smatteo.pv.it

Maria Ruffoli, MD, Pediatric Surgery Unit, Fondazione IRCCS Policlinico San Matteo, Pavia,
Italy.

Ivan Aloï, MD, General and Thoracic Surgery Unit, Department of Surgery, Bambino Gesù
Children's Hospital, IRCCS, Rome, Italy.

Simone Frediani, MD, General and Thoracic Surgery Unit, Department of Surgery, Bambino
Gesù Children's Hospital, IRCCS, Rome, Italy. simone.frediani@opbg.net

Marco Gasparella, MD, Pediatric Surgery Unit, Ca Foncello Hospital-Treviso, Women's and
Children's Health Department, University of Padova-Italy. marco.gasparella@unipd.it

Prof. Paola Midrio, MD, Pediatric Surgery Unit, Ca Foncello Hospital-Treviso, Women's and
Children's Health Department, University of Padova-Italy. paola.midrio@unipd.it

Mohit Kakar, MD PhD, Department of Pediatric Surgery, Riga Stradins University &
Children's Clinical University Hospital. Riga, Latvia. mohitez@gmail.com

Shireen A Nah, MBBS, MRCS, MSurg, Division of Paediatric Surgery, Department of
Surgery, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia.

shireen.nah@ummc.edu.my

Yohesuwary Gunarasa, MD, MRCS, Division of Paediatric Surgery, Department of Surgery, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia.

g.yohesuwary@ummc.edu.my

Toni Risteski, MD PhD, University Clinic of Paediatric Surgery, Medical Faculty, Ss. Cyril and Methodius University, Skopje, R. Macedonia. drtonirist@yahoo.com

Vesna Naunova Cvetanoska, MD, University Clinic of Paediatric Surgery, Medical Faculty, Ss. Cyril and Methodius University, Skopje, R. Macedonia.

Lazo Jovcheski, MD, University Clinic of Paediatric Surgery, Medical Faculty, Ss. Cyril and Methodius University, Skopje, R. Macedonia

Kjetil Juul Stensrud, MD, PhD, Department of Pediatric Surgery, Oslo University Hospital, Oslo, Norway. kstensru@ous-hf.no

Henrik Røkkum, MD, Department of Pediatric Surgery, Oslo University Hospital, Oslo, Norway. b26425@ous-hf.no

Pål Aksel Næss, MD, PhD, Professor, Department of Traumatology, Oslo University Hospital and Institute of Clinical Medicine, University of Oslo. PAANAE@ous-hf.no

Aline Vaz-Silva, MD, MSc, Pediatric Surgery Department, Hospital Dona Estefânia, Centro Hospitalar Universitário de Lisboa Central. alineaazsilva@gmail.com

Joana Patena Forte, MD, Pediatric Surgery Department, Hospital Dona Estefânia, Centro Hospitalar Universitário de Lisboa Central.

Pedro F. Morais, MD, Pediatric Surgery Department, Hospital Dona Estefânia, Centro Hospitalar Universitário de Lisboa Central

Joana Queirós Pereira, MD, Pediatric Surgery Department, Hospital Dona Estefânia, Centro Hospitalar Universitário de Lisboa Central

Prof. Sanja Sindjic Antunovic, MD PhD, University Children's Hospital, Belgrade, Serbia.

sanja.sindjic.antunovic@gmail.com

Prof. Marija Lukac, MD PhD, University Children's Hospital, Belgrade, Serbia

Marion Arnold, MBChB, MMed (Paediatric Surgery), Division of Paediatric Surgery, Red Cross War Memorial Children's Hospital/ University of Cape Town, Cape Town, South Africa.

marion.arnold@uct.ac.za

Martina Ichino [MD]– 1.Division of Paediatric Surgery, Red Cross War Memorial Children's Hospital/ University of Cape Town, Cape Town, South Africa; 2. Department of Pediatric Surgery, Fondazione IRCCS Ca'Granda Ospedale Maggiore Policlinico di Milano, Milan, Italy. martina.ichino@outlook.it

Andrew Victor Bernstein [MBChB]- Division of Paediatric Surgery, Red Cross War Memorial Children's Hospital/ University of Cape Town, Cape Town, South Africa

Hettie le Roux [MBChB]- Division of Paediatric Surgery, Red Cross War Memorial Children's Hospital/ University of Cape Town, Cape Town, South Africa. hettie85@gmail.com

Prof. Leopoldo Martinez, MD PhD, Department of Pediatric Surgery, La Paz Children's Hospital, Madrid, Spain. leopoldo.martinez@salud.madrid.org

Carlos Delgado-Miguel, MD, Department of Pediatric Surgery, La Paz Children's Hospital, Madrid, Spain. carlosdelgado84@hotmail.com

Paolo Bragagnini Rodriguez. Attending Pediatric Surgeon, Department of pediatric Surgery at the University Hospital "Miguel Servet", Zaragoza, Spain (Hospital Universitario Miguel Servet, Zaragoza, España). polobraga@gmail.com

Paula Salcedo Arroyo. Fellow pediatric Surgeon, Department of pediatric Surgery at the University Hospital "Miguel Servet", Zaragoza, Spain (Hospital Universitario Miguel Servet, Zaragoza, España)

Yurema Gonzalez Ruiz. Attending Pediatric Surgeon, Department of pediatric Surgery at the University Hospital "Miguel Servet", Zaragoza, Spain (Hospital Universitario Miguel Servet, Zaragoza, España)

Anna Svenningsson, MD PhD, Department of Pediatric Surgery, Astrid Lindgren Children's Hospital, Karolinska University Hospital, Stockholm, Sweden

Joep PM Derikx, MD PhD, Emma Children's Hospital, Amsterdam UMC, University of Amsterdam & Vrije Universiteit Amsterdam, Department of Pediatric Surgery, Amsterdam, The Netherlands. j.derikx@amsterdamumc.nl

Roel Bakx, MD PhD, Emma Children's Hospital, Amsterdam UMC, University of Amsterdam & Vrije Universiteit Amsterdam, Department of Pediatric Surgery, Amsterdam, The Netherlands. r.bakx@amsterdamumc.nl

Prof. Rene MH Wijnen, MD PhD, Department of Pediatric Surgery and Pediatric Intensive Care, Erasmus University Medical Centre -Sophia Children's Hospital, Rotterdam, The Netherlands. r.wijnen@erasmusmc.nl

Claudia MG Keyzer, MD PhD, Department of Pediatric Surgery and Pediatric Intensive Care, Erasmus University Medical Centre -Sophia Children's Hospital, Rotterdam, The Netherlands. c.keyzer-dekker@erasmusmc.nl

Gerda W Zijp, MD, Pediatric Surgery, Juliana Children's Hospital/Haga-Hospital, The Hague, The Netherlands. g.zijp@hagaziekenhuis.nl

EA Huurman, MD, Pediatric Surgery, Juliana Children's Hospital/Haga-Hospital, The Hague, The Netherlands. eahuurman@live.nl

Prof. Wim van Gemert, MD PhD, Department of Pediatric Surgery, Maastricht UMC, Maastricht, Netherlands. wim.van.gemert@mumc.nl

Olivier Theeuws, MD, Department of Paediatric Surgery, Maastricht UMC, Maastricht, Netherlands. Olivier.theeuws@mumc.nl

Prof Ivo de Blaauw, MD PhD, Department of Pediatric Surgery, Radboud University Medical Center, Amalia Children's Hospital, Nijmegen, The Netherlands.

ivo.deblaauw@radboudumc.nl

Sanne MBI Botden, MD PhD, Department of Pediatric Surgery, Radboud University Medical Center, Amalia Children's Hospital, Nijmegen, The Netherlands.

Sanne.Botden@radboudumc.nl

Maja Joosten, MD, Department of Pediatric Surgery, Radboud University Medical Center, Amalia Children's Hospital, Nijmegen, The Netherlands. maja.joosten@radboudumc.nl

Evert-Jan Boerma, MD PhD, Abdominal Surgery, Zuyderland Medical Centre, Heerlen&Sittard-Geleen, The Netherlands. e.boerma@zuyderland.nl

Donald Schweitzer, MD, Abdominal Surgery, Zuyderland Medical Centre, Heerlen&Sittard-Geleen, The Netherlands. donald.schweitzer@icloud.com

Osman Uzunlu, MD PhD, Department of Pediatric Surgery, Pamukkale University School of Medicine, Denizli, Turkey. osmanuzunlu@gmail.com

Ingo Jester, MD, Department of Paediatric Surgery, Birmingham Children's Hospital, Birmingham, West Midlands, United Kingdom. ingo.jester@nhs.net

Ben Martin, MB BChir, Department of Paediatric Surgery, Birmingham Children's Hospital, Birmingham, West Midlands, United Kingdom. benmartin24@gmail.com

Hetal N Patel, MD, Department of Paediatric Surgery, Birmingham Children's Hospital, Birmingham, West Midlands, United Kingdom. hetalkumarpatel@nhs.net

Dina Fouad, MD, Department of Paediatric Surgery and Urology, Southampton Children's Hospital, Southampton, United Kingdom. Dina.Fouad@uhs.nhs.uk

Christine Lam, MD, Department of Paediatric Surgery and Urology, Southampton Children's Hospital, Southampton, United Kingdom. Christine.Lam@uhs.nhs.uk

Clint D. Cappiello, MD, FACS, Division of Pediatric Surgery, Department of Surgery, The Johns Hopkins Hospital Bloomberg Children's Center, Baltimore, MD, United States of America. ccappie1@jhmi.edu

Carla Lopez, MD, Division of Pediatric Surgery, Department of Surgery, The Johns Hopkins Hospital Bloomberg Children's Center, Baltimore, MD, United States of America.
clopez23@jhmi.edu

Veronica Natale, MPH, Division of Quality and Safety, Department of Pediatrics, The Johns Hopkins University School of Medicine, Baltimore, MD, United States of America.
vnatale1@jhu.edu

Emily Lee, BS, Krieger School of Arts and Sciences, The Johns Hopkins University, Baltimore, MD, United States of America. elee151@jhu.edu

References

1. England RCoSo. Guidance for surgeons working during the COVID-19 pandemic from the Surgical Royal Colleges of the United Kingdom and Ireland. Accessed September 13, 2021,
2. Pelizzo G, Costanzo S, Maestri L, et al. The Challenges of a Children's Hospital during the COVID-19 Pandemic: The Pediatric Surgeon's Point of View. *Pediatr Rep*. Nov 12 2020;12(3):114-123. doi:10.3390/pediatric12030025
3. Surgeons SoAGaE. SAGES and EAES Recommendations Regarding Surgical Response to COVID-19 Crisis. 2020;
4. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet*. Oct 20 2007;370(9596):1453-7. doi:10.1016/s0140-6736(07)61602-x
5. Bhangu A, Søreide K, Di Saverio S, Assarsson JH, Drake FT. Acute appendicitis: modern understanding of pathogenesis, diagnosis, and management. *Lancet*. Sep 26 2015;386(10000):1278-1287. doi:10.1016/s0140-6736(15)00275-5
6. Knaapen M, Hall NJ, Moulin D, et al. International Core Outcome Set for Acute Simple Appendicitis in Children: Results of A Systematic Review, Delphi Study, and Focus Groups with Young People. *Ann Surg*. Dec 29 2020;doi:10.1097/sla.0000000000004707
7. O'Hara LM, Thom KA, Preas MA. Update to the Centers for Disease Control and Prevention and the Healthcare Infection Control Practices Advisory Committee Guideline for the Prevention of Surgical Site Infection (2017): A summary, review, and strategies for implementation. *Am J Infect Control*. Jun 2018;46(6):602-609. doi:10.1016/j.ajic.2018.01.018
8. St Peter SD, Sharp SW, Holcomb GW, 3rd, Ostlie DJ. An evidence-based definition for perforated appendicitis derived from a prospective randomized trial. *J Pediatr Surg*. Dec 2008;43(12):2242-5. doi:10.1016/j.jpedsurg.2008.08.051
9. Delgado-Miguel C, Muñoz-Serrano AJ, Miguel-Ferrero M, De Ceano-Vivas M, Calvo C, Martínez L. Complicated Acute Appendicitis during COVID-19 Pandemic: The Hidden Epidemic in Children. *Eur J Pediatr Surg*. Feb 22 2021;doi:10.1055/s-0041-1723992
10. Fisher JC, Tomita SS, Ginsburg HB, Gordon A, Walker D, Kuenzler KA. Increase in Pediatric Perforated Appendicitis in the New York City Metropolitan Region at the Epicenter of the COVID-19 Outbreak. *Ann Surg*. Mar 1 2021;273(3):410-415. doi:10.1097/sla.0000000000004426
11. Gerall CD, DeFazio JR, Kahan AM, et al. Delayed presentation and sub-optimal outcomes of pediatric patients with acute appendicitis during the COVID-19 pandemic. *J Pediatr Surg*. May 2021;56(5):905-910. doi:10.1016/j.jpedsurg.2020.10.008
12. La Pergola E, Sgrò A, Rebosio F, et al. Appendicitis in Children in a Large Italian COVID-19 Pandemic Area. *Front Pediatr*. 2020;8:600320. doi:10.3389/fped.2020.600320
13. Schäfer FM, Meyer J, Kellnar S, et al. Increased Incidence of Perforated Appendicitis in Children During COVID-19 Pandemic in a Bavarian Multi-Center Study. *Front Pediatr*. 2021;9:683607. doi:10.3389/fped.2021.683607
14. Theodorou CM, Beres AL, Nguyen M, et al. Statewide Impact of the COVID Pandemic on Pediatric Appendicitis in California: A Multicenter Study. *J Surg Res*. Nov 2021;267:132-142. doi:10.1016/j.jss.2021.05.023
15. Hsu YJ, Fu YW, Chin T. Seasonal variations in the occurrence of acute appendicitis and their relationship with the presence of fecaliths in children. *BMC Pediatr*. Nov 16 2019;19(1):443. doi:10.1186/s12887-019-1824-9
16. Sippola S, Grönroos J, Sallinen V, et al. A randomised placebo-controlled double-blind multicentre trial comparing antibiotic therapy with placebo in the treatment of uncomplicated acute appendicitis: APPAC III trial study protocol. *BMJ Open*. Nov 3 2018;8(11):e023623. doi:10.1136/bmjopen-2018-023623

17. Köhler F, Acar L, van den Berg A, et al. Impact of the COVID-19 pandemic on appendicitis treatment in Germany-a population-based analysis. *Langenbecks Arch Surg*. Mar 2021;406(2):377-383. doi:10.1007/s00423-021-02081-4
18. Neufeld MY, Bauerle W, Eriksson E, et al. Where did the patients go? Changes in acute appendicitis presentation and severity of illness during the coronavirus disease 2019 pandemic: A retrospective cohort study. *Surgery*. Apr 2021;169(4):808-815. doi:10.1016/j.surg.2020.10.035
19. Tankel J, Keinan A, Blich O, et al. The Decreasing Incidence of Acute Appendicitis During COVID-19: A Retrospective Multi-centre Study. *World J Surg*. Aug 2020;44(8):2458-2463. doi:10.1007/s00268-020-05599-8

Table 1. Diagnostic work-up, treatment, and outcomes

Characteristics	COVID-19 group (n= 4113)	Control group (n= 4480)	Difference in proportions (95%CI)	p-value
Severity of appendicitis				
- Simple	1973 (48.0%)	2229 (49.8%)		
- Complex	1962 (47.7%)	2017 (45.0%)	2.7% (0.6 to 4.8%)	0.014
- Non-inflamed	168 (4.1%)	220 (4.9%)		
<i>Missing values</i>	<i>10 (0.2%)</i>	<i>14 (0.3%)</i>		
Patients screened for COVID-19			-	-
- Yes	3095 (75.2%)	-		
- No	997 (24.2%)	-		
<i>Missing values</i>	<i>21 (0.5%)</i>	-		
Test results				
- Test positive	71 (1.7%)	-		
- Test negative	2998 (72.9%)	-		
Inconclusive/unknown	26 (0.6%)	-		
No. of patients that underwent diagnostic imaging, n (%)	3535 (86.0%)	3780 (84.4%)	1.6% (0.1 to 3.1%)	0.04
Type of imaging, n (%)			-	-
- Ultrasound (US)	3205 (77.9%)	3450 (77.0%)		
- MRI	9 (0.2%)	5 (0.1%)		
- CT	88 (2.1%)	66 (1.5%)		
- US + MRI	59 (1.4%)	63 (1.4%)		
- US + CT	161 (3.9%)	164 (3.7%)		
- MRI + CT	1 (<0.1%)	1 (<0.1%)		
- US + MRI + CT	1 (<0.1%)	3 (0.1%)		
- <i>Missing</i>	<i>11 (0.3%)</i>	<i>28 (0.6%)</i>		
Treatment strategy				
- Non-operative treatment	316 (7.7%)	327 (7.3%)	0.4% (-0.7 to 1.5%)	0.50
- Surgical treatment	3797 (92.3%)	4153 (92.7%)	0.4% (-0.7 to 1.5%)	0.48
Surgical approach				
- Laparoscopic	2748 (66.8%)	2889 (64.5%)	2.3% (0.3 to 4.3%)	0.03

- Open	967 (23.5%)	1191 (26.6%)	3.1% (1.3 to 4.9%)	0.001
- Laparoscopic converted to open	75 (1.8%)	69 (1.5%)	-	-
- Other	7 (0.2%)	4 (0.1%)	-	-
Negative appendectomy	168 (4.1%)	220 (4.9%)	0.8% (-0.8 to 1.7%)	0.08
<i>Missing</i>	10 (0.2%)	14 (0.3%)		
Initial length of stay (d), median (IQR)	3 (2-6)	3 (2-6)	-	0.75
<i>Missing</i>	2 (<0.1%)	41 (0.9%)		
Total length of stay (d), median (IQR)	4 (2-6)	4 (2-6)	-	0.37
<i>Missing</i>	2 (<0.1%)	42 (0.9%)		
Hospital readmission	226 (5.5%)	232 (5.2%)	0.3% (-0.7 to 1.3%)	0.53
<i>Missing</i>	5 (0.1%)	4 (0.1%)		
No. of patients with a complication	478 (11.6%)	496 (11.1%)	0.5% (-0.8 to 1.8%)	0.43
<i>Missing</i>	4 (0.1%)	8 (0.2%)		
Patients with a minor complication (CD I-II)	325 (7.9%)	323 (7.2%)	0.7% (-0.4 to 1.8%)	0.22
Patients with a severe complication (CD III-IV)	149 (3.6%)	168 (3.7%)	0.1% (-0.7 to 0.9%)	0.81
Death (CD V)	1 (<0.1%)	1 (<0.1%)	0% (-0.1 to 0.1%)	>0.99
<i>Missing</i>	8 (0.2%)	12 (0.3%)		
Type of complication			-	-
- Intra-abdominal abscess	254 (6.2%)	242 (5.4%)		
- Surgical Site Infection	110 (2.7%)	102 (2.3%)		
- Small bowel obstruction	52 (1.3%)	43 (1.0%)		
Need for reoperation	72 (1.8%)	102 (2.3%)	0.5% (-0.1 to 1.1%)	0.08
No. of patients with at least one outpatient visit	1898 (46.1%)	2791 (62.3%)	16.2% (14.1 to 18.3%)	<0.001
<i>Missing</i>	3	6		
No. of patients with a telephone check-up	777 (18.9%)	416 (9.3%)	9.6% (8.1 to 11.1%)	<0.001
<i>Missing</i>	5 (0.1%)	11 (0.2%)		

Data is displayed as count (percentage of total)

Table 2. Subgroup analyses on severity of appendicitis and complications

Characteristics	COVID-19 group (n= 4113)	Control group (n= 4480)	Difference in proportions (95%CI)	Adjusted p-value
Patients treated for complex appendicitis				
Time period				
- First three months	672/1287 (52.2%)	669/1436 (46.6%)	5.6% (1.8 to 9.3%)	0.007
- Rest of the year	1290/2816 (45.8%)	1348/3030 (44.5%)	1.3% (-1.3 to 3.9%)	0.64
<i>Missing</i>	10	14		
Age				
- <6 years old	357/501 (71.3%)	399/590 (67.6%)	3.7% (-1.8 to 9.1%)	0.56
- 6-12 years old	1018/2227 (45.7%)	1025/2354 (43.5%)	2.2% (-0.7 to 5.1%)	0.40
- >12 years old	587/1375 (42.7%)	593/1522 (39.0%)	3.7% (0.1 to 7.3%)	0.13
<i>Missing</i>	10	14		
Region				
- Europe	1632/3406 (47.9%)	1593/3585 (44.4%)	3.5% (1.2 to 5.8%)	0.02
- North-America	136/334 (40.7%)	154/355 (43.4%)	2.7% (-4.7 to 10.0%)	>0.99
- South-America	22/47 (46.8%)	59/102 (57.8%)	11.0% (-6.0 to 27.3%)	0.63
- Africa	86/117 (73.5%)	108/157 (68.8%)	4.7% (-6.3 to 15.2%)	>0.99
- Asia	86/199 (43.2%)	103/267 (38.6%)	4.6% (-4.4 to 13.5%)	0.95
<i>Missing</i>	10	14		
Subgroup analysis on patients experiencing a complication				
Time period				
- First three months	176/1291 (13.6%)	173/1435 (12.1%)	1.5% (-1.0 to 4.0%)	0.48
- Rest of the year	302/2818 (10.7%)	323/3037 (10.6%)	0.1% (-1.5 to 1.7%)	>0.99
<i>Missing</i>	4	8		
Age				
- <6 years old	75/503 (14.9%)	100/589 (17.0%)	2.1% (-2.3 to 6.4%)	>0.99
- 6-12 years old	246/2230 (11.0%)	252/2361 (10.7%)	0.3% (-1.5 to 2.1%)	>0.99
- >12 years old	157/1376 (11.4%)	144/1522 (9.5%)	1.9% (-0.3 to 4.2%)	0.28

<i>Missing</i>	4	8		
Region				
- Europe	404/3408 (11.9%)	386/3592 (10.7%)	1.2% (-0.2 to 2.7%)	0.57
- North-America	28/334 (8.4%)	34/354 (9.6%)	1.2% (-3.2 to 5.5%)	>0.99
- South-America	5/47 (10.6%)	24/102 (23.5%)	12.9% (-1.0 to 23.8%)	0.33
- Africa	24/121 (19.8%)	32/157 (20.4%)	0.6% (-9.1 to 9.9%)	>0.99
- Asia	17/199 (8.5%)	20/267 (7.5%)	1.0% (-3.9 to 6.4%)	>0.99
<i>Missing</i>	4	8		

Data is displayed as count (percentage of total)

Supplement 1. Definition of COVID period and healthcare regulations

Country	Site	Number of patients	Start date COVID-19	NOT standard of care	Same day discharge standard of care	Shift of patients with acute appendicitis
<u>Austria</u>	Graz	352	March 2020	No	No	No
	Vienna	224	March 2020	No	No	COVID+ patients were referred to another hospital
<u>Bangladesh</u>	Dhaka	56	March 2020	No	No	No
<u>Belgium</u>	Brussels	120	March 2020	No	No	No
	Leuven	161	March 2020	No	No	No
<u>Brazil</u>	Sao Paolo	149	March 2020	No	No	No
<u>Canada</u>	Toronto	511	April 2020	No	No	No
<u>Denmark</u>	Odense	171	March 2020	No	No	No
<u>Finland</u>	Helsinki	279	March 2020	No	No	No
<u>France</u>	Angers	235	March 2020	No	No	No
	Paris	328	March 2020	No	Yes	Patients (both simple and complex appendicitis) were referred from peripheral hospitals to this hospital due to reduced OR capacity
<u>Israel</u>	Ber Sheva	292	April 2020	No	No	No
<u>Italy</u>	Alessandria	103	March 2020	No	Yes	No
	Brescia	289	March 2020	Yes	No	No
	Florence	242	March 2020	No	Yes	No
	Messina	150	March 2020	No	No	COVID+ patients were referred to another hospital
	Padua	106	March 2020	No	No	No
	Pavia	96	March 2020	No	No	Patients (both simple and complex appendicitis) were referred from peripheral hospitals to this hospital
	Rome	528	March 2020	No	No	No
	Treviso	146	February 2020	No	No	No
<u>Latvia</u>	Riga	191	February 2020	Yes	No	No

<u>Malaysia</u>	Kuala Lumpur	27	February 2020	No	No	No
<u>North-Macedonia</u>	Skopje	244	March 2020	No	No	No
<u>Norway</u>	Oslo	208	March 2020	No	No	No
<u>Portugal</u>	Lisbon	580	March 2020	No	No	No
<u>Serbia</u>	Belgrade	307	March 2020	No	No	Patients (both simple and complex appendicitis) were referred from peripheral hospitals to this hospital
<u>South-Africa</u>	Cape Town	278	March 2020	Yes	No	All pediatric cases were referred to this hospital
<u>Spain</u>	Madrid	554	March 2020	No	No	Emergency pediatric surgery was concentrated in this hospital
	Zaragoza	387	March 2020	No	No	No
<u>Sweden</u>	Stockholm	297	March 2020	Yes	No	No
<u>The Netherlands</u>	Amsterdam	29	March 2020	No, only in trial setting	No	No
	Heerlen	117	March 2020	No, only in trial setting	No	No
	Maastricht	45	March 2020	No	No	No
	Nijmegen	7	March 2020	No	No	No
	Rotterdam	33	March 2020	No	No	No
	The Hague	145	March 2020	No, only in trial setting	No	No
<u>Turkey</u>	Denizli	91	March 2020	Yes	No	No
<u>United Kingdom</u>	Birmingham	196	April 2020	No	No	No
	Southampton	141	April 2020	No, surgeon discretion	No	No
<u>United States</u>	Baltimore	178	April 2020	Yes	Yes	COVID+ cases were transferred to this hospital

Non-operative treatment protocols:

Brescia, Italy: Intravenous (IV) ceftriaxone for 7 days in case of simple appendicitis, ceftriaxone + metronidazole IV for complicated appendicitis.

Riga, Latvia: IV ampicillin + metronidazole for 72 hours followed by 7 days oral augmentin to complete a course of 10 days. Discharge criteria: Clinical improvement, decreased c-reactive protein, and no deterioration on repeat ultrasound.

Cape Town, South-Africa: IV augmentin for 24-48 hours followed by oral augmentin + amoxicillin to complete a course of 10 days. Discharge criteria: Clinical improvement and after confirmation that caregivers have clear understanding of symptoms to prompt early return to hospital as well as easy access to transport back to the hospital.

Stockholm, Sweden: IV piperacillin/tazobactam for 24 hours followed by oral ciprofloxacin + metronidazole to complete a course of 10 days. Discharge criteria: Clinical improvement after 24 to 48 hours.

All centers, The Netherlands: IV augmentin + gentamicin for 48 hours followed by 5 days oral augmentin. Discharge criteria: Clinical improvement, decreased leukocytes and c-reactive protein and no deterioration on repeat ultrasound.

Denizli, Turkey: IV ampicillin/sulbactam + gentamicin + clindamycin for 5 days followed by oral augmentin + metronidazole to complete a course of 10 days.

Southampton, United Kingdom: No written protocol, but a minimum of 24 hours of IV antibiotics.

Baltimore, United States: IV ceftriaxone + metronidazole for at least 24 hours followed by oral Levaquin + metronidazole to complete a course of 10-14 days. Discharge criteria: toleration of oral diet, afebrile, pain improved. In case of complicated appendicitis interval appendectomy was planned 6 to 8 weeks after discharge.

Supplement 2. Outcomes and definitions

Secondary outcomes

Children developing complex appendicitis after non-operative treatment (NOT): The proportion of children that were initially treated non-operatively for simple appendicitis and subsequently developed complex appendicitis (either during initial admission or due to recurrence of disease) within 30 days after initial treatment.

Children with recurrent appendicitis after NOT: Recurrent appendicitis was defined as histopathological confirmed acute appendicitis within 30 days after initial NOT.

Hospital readmissions: The number of patients that were readmitted for a complication related to appendicitis treatment within 30 days after initial treatment.

Need for reoperation: The number of patients that underwent a second surgical procedure in the same site for the same indication within 30 days after primary appendectomy.

Length of hospital stay: The total duration of hospital stay during the first admission (initial length of hospital stay) combined with admission due to complications related to appendectomy or appendicitis.

Number of outpatient visits: The number of regular visits and telephone check-ups related to appendicitis treatment.

Other definitions

Non-operative treatment (NOT): Non-operative treatment of simple appendicitis consisted of a minimum of 24 hours intravenous antibiotics with or without a subsequent course of oral antibiotics, according to local protocol. Non-operative treatment of complex appendicitis consisted of intravenous antibiotics with or without percutaneous drainage (in case of appendiceal abscess).

Successful NOT: Successful NOT was defined as no need for appendectomy during the 30-day follow-up period of the study.

Simple appendicitis: Simple appendicitis was defined as the macroscopic appearance of an increased diameter of the appendix and microscopic transmural inflammation, ulceration, or thrombosis, without signs of necrosis or perforation.⁶

Complex appendicitis: Complex appendicitis was defined as appendicitis with macroscopic or microscopic signs of transmural inflammation with necrosis (gangrenous appendicitis) or perforation, or appendicitis with abscess or mass.⁶

Appendiceal perforation: Perforation was defined as a visible hole in the appendix or a free fecalith in the abdominal cavity.⁷

Intra-abdominal abscess (IAA): IAA was defined as a radiologically confirmed accumulation of purulent fluid in a walled-off space within the abdominal cavity.

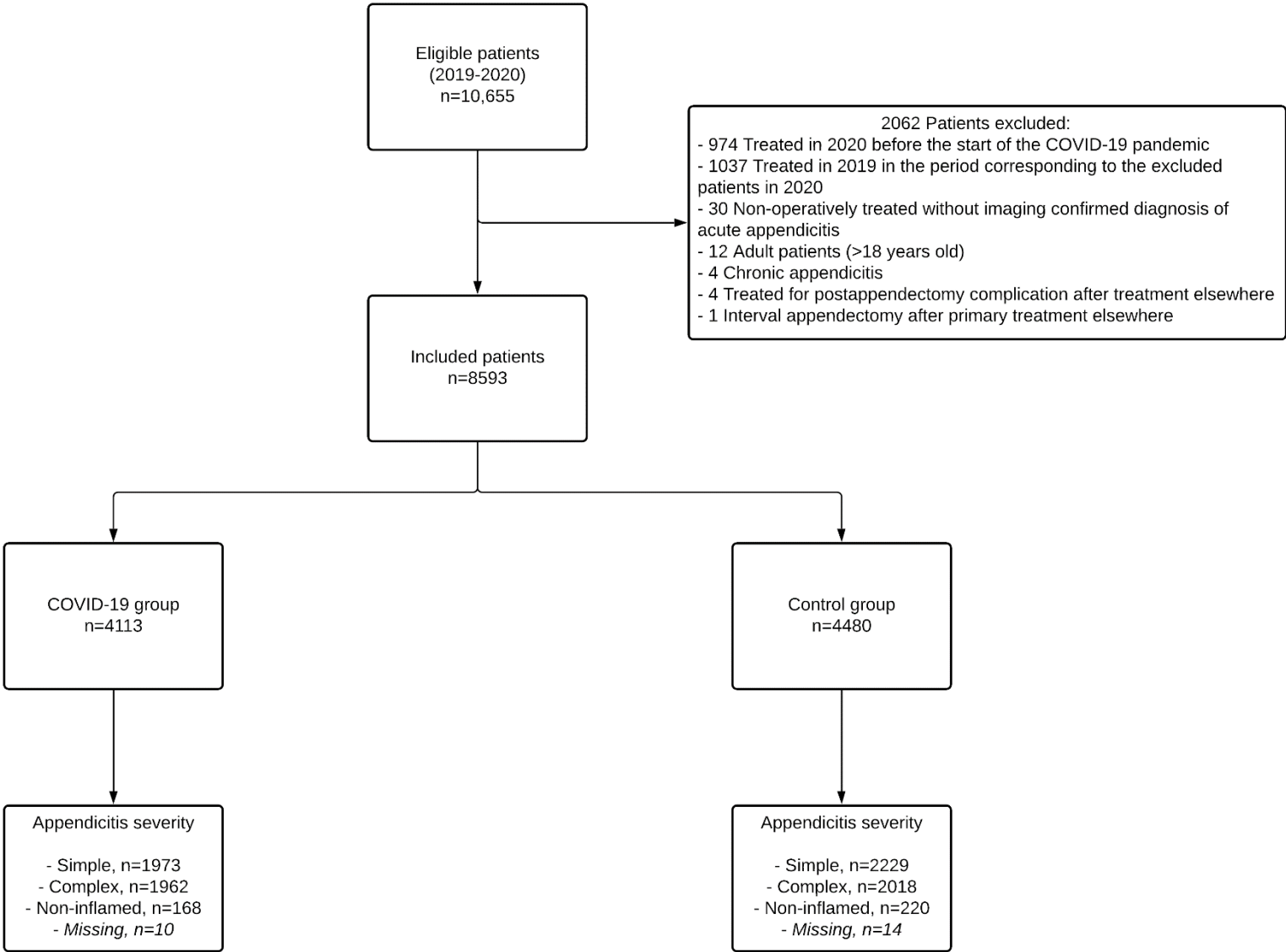
(Adhesive) bowel obstruction: The diagnosis of (adhesive) bowel obstruction was based on clinical signs and symptoms such as history of constipation, nausea, vomiting, and distended abdomen.

Surgical site infection (SSI): Superficial and deep SSI were defined according to the CDC criteria.⁸

Supplement 3. Survey: Changes in healthcare protocols and treatment of appendicitis

1. Please indicate the start date of the COVID-19 pandemic in your region (based on the start of the time period in which healthcare in your hospital was affected by the pandemic)
2. Did you experience different peaks in the number of patients treated for COVID-19 in your hospital? If so, please define the start and end dates of these COVID-19 peaks.
3. Please indicate the percentage of reduced operation room capacity in your hospital during the COVID-19 pandemic
4. Did your hospital change any surgical healthcare protocols regarding the treatment of acute appendicitis during the COVID-19 pandemic?
5. Was non-operative treatment preferred for children with simple appendicitis according your adjusted protocol?
6. Was same day discharge preferred for children with simple appendicitis according to your adjusted protocol?
7. Did the changes in surgical protocols and/or reduction of operation room capacity affect the treatment of children with acute appendicitis in any other way?
8. Were any healthcare protocols implemented in your country that ordered a shift in appendicitis treatment from tertiary (academic) hospitals to peripheral hospitals or vice versa?
9. If so, did this shift of patients affect treatment of children with appendicitis in your hospital? Did your hospital treat more or less children with acute appendicitis due to the adjusted healthcare protocols?
10. Do you have any additional comments regarding changes in your healthcare protocols and management strategies for acute appendicitis during the COVID-19 pandemic?

Supplement 4. Patient flowchart



Supplement 5. Baseline characteristics

Characteristics	COVID-19 group (n= 4113)	Control group (n= 4480)	p-value
Age, y*	9.8 ± 3.6	9.9 ± 3.7	0.55
Male sex	2558 (62.2%)	2689 (60.0%)	0.04
Days abdominal pain^	1 (1-2)	1 (1-2)	0.41
<i>Missing values</i>	36	62	
Temperature at presentation*	37.2 ± 0.9	37.2 ± 0.9	0.09
<i>Missing values</i>	138	151	
Leukocytes*	15.1 ± 5.5	15.1 ± 5.6	0.61
<i>Missing values</i>	136	184	
CRP^	24.0 (5.0-73.0)	20.0 (3.6-67.9)	0.001
<i>Missing values</i>	160	231	
Severity of appendicitis			0.02
- Simple	1973 (48.0%)	2229 (49.8%)	
- Complex	1962 (47.7%)	2017 (45.0%)	
- Non-inflamed	168 (4.1%)	220 (4.9%)	
<i>Missing values</i>	10 (0.2%)	14 (0.3%)	
Patients screened for COVID-19			-
- Yes	3095 (75.2%)	-	
- No	997 (24.2%)	-	
<i>Missing values</i>	21 (0.5%)	-	
Test results			
- Test positive	71 (1.7%)	-	
- Test negative	2998 (72.9%)	-	
Inconclusive/unknown	26 (0.6%)	-	

Data displayed as count (percentage of total group count)

*Data displayed as mean ± standard deviation

^Data displayed as median (interquartile range)

Supplement 6a. Outcomes of NOT for simple appendicitis

Characteristics	COVID-19 group (n=211)	Control group (n=208)
Need for appendectomy within one month	27 (12.8%)	27 (13.0%)
Reason for appendectomy		
- Primary failure of NOT	17 (8.1%)	19 (9.1%)
- Recurrent appendicitis	10 (4.7%)	7* (3.4%)
Patients developing complex appendicitis	9 (4.3%)	2 (1.0%)
- Primary	7 (3.3%)	2 (1.0%)
- Secondary	2 (0.9%)	0

* One patient with a suspicion of recurrent appendicitis had a non-inflamed appendix at histopathological examination

Data is displayed as count (percentage of total)

Supplement 6b. Outcomes of NOT for complex appendicitis

Characteristics	COVID-19 group (n=105)	Control group (n=119)
Indication for NOT		
- Appendix mass	26 (24.8%)	33 (27.7%)
- Appendiceal abscess	63 (60.0%)	70 (58.8%)
- Unknown	16 (15.2%)	16 (13.4%)
Need for appendectomy within one month	14 (13.3%)	18 (15.1%)
Reason for appendectomy		
- Primary failure of NOT	6 (5.7%)	8 (6.7%)
- Recurrent appendicitis	7 (6.7%)	8 (6.7%)
- Interval appendectomy	0	2 (1.7%)
<i>Missing</i>	<i>1 (1.0%)</i>	<i>0</i>

Data is displayed as count (percentage of total for each subgroup)